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(WO/2001/054733) NUCLEIC ACIDS, PROTEINS AND ANTIBODIES

Biblio. Data	Description	Claims	National Phase	Notices	Documents
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Note: OCR Text

Nucleic Acids, Proteins, and Antibodies [1] This application refers to a "Sequence Listing" that is provided only on electronic media in computer readable form pursuant to Administrative Instructions Section 801 (a) (f).

The Sequence Listing forms a part of this description pursuant to Rule 5. 2 and Administrative Instructions Sections 801 to 806, and is hereby incorporated in its entirety.

[2] The Sequence Listing is provided as an electronic file (PTZ32PCTseqList.txt, 3, 411, 276 bytes in size, created on January 13, 2001) on four identical compact discs (CD- R), labeled "COPY 1," "COPY 2," "COPY 3," and "CRF." The Sequence Listing complies with Annex C of the Administrative Instructions, and may be viewed, for example, on an IBM-PC machine running the MS-Windows operating system by using the V viewer software, version 2000 (see World Wide Web URL : <http://www.flieviewer.com>).

Field of the Invention [3] The present invention relates to novel proteins. More specifically, isolated nucleic acid molecules are provided encoding novel polypeptides. Novel polypeptides and antibodies that bind to these polypeptides are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human polynucleotides and/or polypeptides, and antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to these novel polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further relates to methods and/or compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.

Background of the Invention [4] One of the most critical tasks a cell must perform is to respond to cues from its environment, i. e., extracellular signals. Some of the most important extracellular signals come from other cells. The ability for cells to be able to send and receive signals from one another is of paramount importance in multicellular organisms because it allows individual cells within a body to become highly specialized and yet work in a coordinated fashion with other cells of the body. Cellular signaling mechanisms regulate a variety of cellular processes such as, for example, proliferation, differentiation, survival, movement, and secretion. Defects in cellular signaling can lead to a number of diseases and disorders such as cancers, immune system disorders and nervous system disorders. For more expansive reviews on this subject, please refer to Hunter, Cell 100 : 113-127 and Chapter 15 of Molecular Biology of the Cell, Third Edition, edited by Alberts et al. (1994), which are herein incorporated by reference in their entirety.

[5] Signal transduction requires molecules that serve as the extracellular signaling molecules as well as a set of receptors that "receive" the signal. Frequently, an additional set of proteins is necessary in order for the cell to transduce the signal it has received into an appropriate response via the activation or inhibition of a particular set of genes or proteins.

The signaling molecules, the receptor proteins, and the molecules that relay the signal between the receptor and the final effector molecules collectively form what are known as signal transduction pathways.

[6] To date, several common types of signal transduction pathways have been identified. One way to classify a signal transduction pathway is based on the class of receptor protein it utilizes. Two well known classes of receptor proteins are G-protein coupled receptors and enzyme-linked receptors. This latter class of enzyme-linked receptors includes receptor tyrosine kinases, tyrosine kinase associated receptors, receptor serine/threonine kinases, receptor tyrosine phosphatases, and receptor guanylyl cyclases.

Signal Transduction through G-protein Coupled Receptors [7] G protein coupled receptors are the largest family of cell surface receptors. They are seven-pass transmembrane receptors which activate trimeric G proteins (G proteins) upon ligand binding. G proteins are GTPases composed of three subunits: alpha, beta and gamma.

G proteins function as molecular switches existing in two states: an active GTP bound state and an inactive GDP bound state. Ligand binding to G protein coupled receptors induce inactive G proteins to release GDP allowing GTP to bind in its place. Binding of GTP to a G protein causes the alpha subunit to dissociate from the beta and gamma subunits which remain associated with one another. Eventually, the GTPase activity of the alpha subunit results in hydrolysis of the bound GTP molecule to GDP, thus inactivating the G protein.

[8] There are several types of G proteins that have been classified based upon their function. Stimulatory G proteins (Gs) are involved in adenylate cyclase activation; inhibitory G proteins (Gi) function to inhibit the activity of adenylate cyclase. Yet another type of G protein, Gq proteins, functions in the activation of phosphoinositide-specific phospholipase C enzyme.

[9] Activation of adenylate cyclase by an activated Gs protein results in the production of the cyclic nucleotide, cyclic AMP (cAMP). cAMP mediates its effects mostly through its activation of cAMP dependent kinase (A-kinase), a serine/threonine kinase. Activation of A-kinase helps to further relay the signal from the G protein coupled receptor to the target proteins. In muscle cells, for instance, activation of A-kinase following adrenaline signaling ultimately results in the activation of an enzyme, glycogen phosphorylase, which catalyzes the release of glucose molecules which can be used to produce energy from glycogen. In other instances, activated A-kinase translocates to the nucleus where it phosphorylates the cAMP response element binding (CREB) protein, which when phosphorylated, acts as a transcription factor to stimulate the expression of genes that have cAMP response elements (CRE) sequences in their regulatory regions.

[10] Gq proteins, when activated, activate the enzyme phospholipase C-beta which hydrolyzes PI 4, 5-bisphosphate (PIP2) producing inositol triphosphate (IP3) and diacylglycerol (DAG). IP3 functions as a second messenger that causes the release of Ca²⁺ from intracellular stores. Released calcium then binds to Ca²⁺ binding proteins such as calmodulin, which in its calcium bound state, is able to activate Ca²⁺/calmodulin dependent protein kinases (CaM-kinases). Activated CaM kinases then continue to relay the signal to more downstream molecules in the signal transduction pathway. The other product produced by phospholipase C-beta, DAG, functions to activate the serine/threonine kinase known as protein kinase C (PKC). Activated PKC phosphorylates target proteins depending on the cell type, and in many cells these phosphorylation events lead to the increased transcription of specific genes. The highest concentrations of protein kinase C are found in the brain where PKC phosphorylates ion channels in nerve cells thereby altering their excitability. PKC activation can be induced by treating cells with phorbol esters which are able to cross the plasma membrane, bind to, and activate PKC directly.

Signal Transduction through Receptor Tyrosine Kinases [11] The receptor protein tyrosine kinases (RPTKs) are some of the most well studied receptors, and the signaling cascades they initiate demonstrate two of the fundamental concepts in signal transduction: the regulation of protein phosphorylation and the recruitment of proteins into a signaling cascade via protein-protein interaction domains.

[12] Binding of the cognate ligand to a RPTK, such as epidermal growth factor (EGF) binding to the epidermal growth factor receptor (EGFR), induces RPTKs to dimerize and cross-phosphorylate each other on multiple tyrosine residues. The phosphorylated receptor dimer is the activated form of the receptor.

[13] The phosphorylated tyrosines on activated RPTKs are then recognized/bound by other components of the signal transduction pathway. One of the important discoveries in the field of signal transduction was the recognition of conserved domains which allow for protein-protein interactions in signaling pathways. The most prevalent binding domain that recognizes phosphotyrosine (P-Tyr) residues is known as the SH2 domain (for Src homology region 2, named after the Src protein in which the SH2 domain was first discovered).

Another domain that recognizes P-Tyr residues is called the P-Tyr binding domain (PTB).

The discovery of the SH2 domain was quickly followed by the discovery of several other protein-protein interaction

domains involved in signal transduction and by the realization that most of these domains are modular in nature, meaning these domains fold independently—a most convenient feature for protein engineering. To date, more than 100 such protein interaction domains involved in signaling have been defined via comparative sequence analysis. Most of these domains recognize short linear sequences (approximately 4-10 amino acid residues in length), in some cases requiring phosphorylation of specific residues within the sequence allowing for inducible association. A convenient web based database, with links to abstracts of papers characterizing these domains can be found at <http://smart.embl-heidelberg.de>.

[14] Proteins containing SH2 and PTB domains translocate to the plasma membrane where they associate with the activated RPTKs which, in turn, activates them through phosphorylation. By way of example, activation of the platelet derived growth factor receptor (PDGFR) results in the autophosphorylation of tyrosine residues in the cytoplasmic tail of the PDGFR. These P-Tyr residues then serve as the binding sites for other proteins, such as a GTPase (discussed in more detail below), phospholipase C-gamma, and the regulatory subunit of PI-3-kinase, which are each able to recognize the P-Tyr residues in PDGFR via SH2 domains. The interaction of these proteins with the activated PDGFR results in the translocation of these proteins to the plasma membranes where they have their substrates and the PDGFR mediated activation of these proteins via phosphorylation.

[15] In the previous example, each of the proteins recruited to the activated RPTK via their SH2 domains also had catalytic activities that allowed them to propagate a signal.

There are proteins involved in signal transduction, however, which have no ability in and of themselves to propagate a signal. Instead, these proteins, known as adaptor proteins, serve to couple activated RPTKs to other components of the signal transduction pathway which do have the capacity to propagate the signal. One such adaptor protein is known as Grb2. It contains one SH2 domain and two SH3 domains (another Src homology domain that mediates protein interactions). Grb 2 is constitutively associated with Sos protein, a guanine nucleotide releasing protein (GNRP), via its SH3 domain. Thus, when Grb2 associates with an activated receptor via its SH2 domain, it also brings Sos into proximity with the RPTK which activates the Sos protein via phosphorylation.

[16] GNRP proteins, such as Sos, are one of two types of proteins that help regulate the activity of proteins belonging to the Ras superfamily of monomeric GTPases. Ras proteins are proteins that are associated with the cytoplasmic side of the plasma membrane and help relay signals from RPTK to the nucleus to stimulate cell proliferation or differentiation. Ras proteins exist in two states, an inactive state in which ras is bound to GDP and an active state in which ras is bound to GTP. Activated GNRP proteins promote the exchange of bound GDP for GTP on ras proteins, thereby activating ras. Ras, itself, is a GTPase that hydrolyzes GTP to GDP, and would therefore tend to inactivate itself over time. However, ras is an inefficient GTPase, so the inactivation of ras is enhanced by GTPase activating proteins (GAPs) which increase the rate of hydrolysis of GTP by ras.

[17] Activated Ras kinases then act to activate more downstream signaling events, including activation of the mitogen-activated protein kinase (MAPK) pathway which is a cascade of serine/threonine kinases. Ras binds to and activates a MAPK kinase kinase (MAPKKK, such as Raz-1, for example), which in turn activates a MAPK kinase (MAPKK) via phosphorylation, which in turn activates a MAPK. MAPKs relay signals downstream by phosphorylating various proteins in the cell including other kinases and/or regulatory proteins in the cell. For instance, an activated MAPK can enter the nucleus and help to initiate transcription of genes that must be expressed in order for the cell to respond to the extracellular signal, such as genes required for DNA replication in response to the extracellular proliferation signal.

[18] Another class of signaling receptors, receptor serine/threonine kinases (RISK) has recently been identified. An example of an RSK is the TGF-beta receptor. Additionally, it has also been recently recognized that there are modular binding domains that recognize phosphoserine/phosphothreonine (P-Ser/P-Thr) residues. For instance, 14-3-3 domains recognize phosphoserines in specific amino acid contexts [RSX (P-Ser) XP] or [R (Y/F) X (P-Ser) XP] and may function in the assembly of signaling complexes. Other residues such as histidine and arginine can also be phosphorylated, and it is possible that additional kinases which phosphorylate these residues, or protein domains that bind phosphohistidine or phosphoarginine will be discovered.

Signaling Via Intracellular Receptors [19] Some extracellular signals do not have cell surface receptors such as G protein coupled receptors or receptor tyrosine kinases. Instead, these extracellular signals are able to traverse the plasma

membrane and interact with their receptors in the cytoplasm. Examples of such signals are the steroid hormones and the gas nitrous oxide (NO). The steroid hormone receptors, once bound by their ligand, are generally able to translocate to the nucleus where they bind regulatory DNA elements that control the gene expression of specific genes. NO gas, on the other hand, generally enters a cell and reacts with iron in the active site of the enzyme guanylate cyclase, stimulating it to produce cyclic GMP (cGMP). cGMP acts as a second messenger (similar to the way cAMP functions) and can stimulate further downstream signaling by binding to other proteins.

Terminating Sig7zai T7 ansduction [20] As the effects of signal transduction are transient, there must also be mechanisms for terminating signal cascades. For example, G proteins are self-inactivating, and there are a set of proteins, GAPs, that are devoted to increasing the rate of hydrolysis of bound GTP by ras proteins. Cyclic nucleotide second messengers such as cAMP and cGMP are hydrolyzed by phosphodiesterases. In the case of kinases, there generally exist a set of complementary phosphatases that function to dephosphorylate phosphorylated residues, thereby bringing the signaling event to a close.

Signal Transduction Pathway Components and Disease [21] Because signal transduction is involved in the regulation of so many cellular processes, including proliferation, differentiation, survival, and apoptosis, it is not surprising that defects in cellular signal transduction pathway components lead to a number of diseases and disorders, especially cancers. For a review on Signal transduction pathway components and diseases, see Hunter, Philosophical Transactions of the Royal Society of London Series B 353 : 583-605 (1998) which is herein incorporated by reference in its entirety. For instance, approximately 30% of human cancers have mutations in a ras gene, and at least 18 tyrosine kinases have been identified as oncogenes in either acutely transforming retroviruses or in human tumors, such as for example, Src. And more than 95% of chronic myelogenous leukemias express an activated form of the c-Abi non-receptor tyrosine kinases.

[22] Mutations in signaling pathways are also implicated in a plethora of other diseases.

Mutation in Bruton's tyrosine kinase leads to X-linked agammaglobulinemia. Inactivation of ZAP70 or JAK3 leads to a severe combined immunodeficiency disease. Coffin-Lowry syndrome occurs when the X-linked Rsk2 protein serine kinase gene is inactivated.

Myotonic dystrophy occurs when expression of the myotonic dystrophy serine kinase gene is decreased. Overexpression of the aurora2 serine kinase is implicated in colon carcinoma.

[23] The malfunction of signal transduction pathway components, particularly kinases, in diseases indicate that these genes are good targets for drugs/pharmaceuticals that either inhibit or activate their function. In fact, some such drugs have been developed and are already in use or in clinical trials. For instance, an inhibitor of cyclin dependent kinase 2 (cdk2), a kinase important in regulating cellular proliferation, is in clinical trials for cancer treatment, as are inhibitors of epidermal growth factor receptor tyrosine kinases and vascular endothelial growth factor receptor (VEGFR) tyrosine kinases. Inhibition of VEGFR activity reduces or eliminates the vascularization of tumors directed by VEGFR. An antagonistic monoclonal antibody, hereceptin, against the erbB2 receptor tyrosine kinase is being used in breast cancer therapies to treat breast cancers where ErbB2 is overexpressed.

[24] Thus there exists a clear need for identifying and exploiting novel signal transduction pathway component polynucleotides and polypeptides. Although structurally related, such proteins may possess diverse and multifaceted functions in a variety of cell and tissue types. The inventive purified signal transduction pathway component polypeptides are research tools useful for the identification, characterization and purification of additional proteins involved in signal transduction. Furthermore, the identification of new signal transduction pathway component polynucleotides and polypeptides permits the development of a range of derivatives, agonists and antagonists at the nucleic acid and protein levels which in turn have applications in the treatment and diagnosis of a range of conditions such as, for example, cancer and other proliferative disorders (e. g., chronic myelogenous leukemia), immunological disorders (e. g., severe combined immunodeficiency and X-linked agammaglobulinemia), and nervous system disorders (Coffin-Lowry Syndrome), amongst other conditions.

Summary of the Invention [25] The present invention relates to novel proteins. More specifically, isolated nucleic acid molecules are provided encoding novel polypeptides. Novel polypeptides and antibodies that bind to these polypeptides

are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human polynucleotides and/or polypeptides, and antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to these novel polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further relates to methods and/or compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.

Detailed Description Tables [26] Table 1A summarizes some of the polynucleotides encompassed by the invention (including cDNA clones related to the sequences (Clone ID NO : Z), contig sequences (contig identifier (Contig ID :) and contig nucleotide sequence identifier (SEQ ID NO : X)) and further summarizes certain characteristics of these polynucleotides and the polypeptides encoded thereby. The first column provides the gene number in the application for each clone identifier. The second column provides a unique clone identifier, "Clone ID NO : Z", for a cDNA clone related to each contig sequence disclosed in Table 1A. The third column provides a unique contig identifier, "Contig ID : " for each of the contig sequences disclosed in Table 1A. The fourth column provides the sequence identifier, "SEQ ID NO : X", for each of the contig sequences disclosed in Table 1A. The fifth column, "ORF (From-To)", provides the location (i.e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO : X that delineate the preferred open reading frame (ORF) that encodes the amino acid sequence shown in the sequence listing and referenced in Table 1A as SEQ ID NO : Y (column 6). Column 7 lists residues comprising predicted epitopes contained in the polypeptides encoded by each of the preferred ORFs (SEQ ID NO : Y). Identification of potential immunogenic regions was performed according to the method of Jameson and Wolf (CABIOS, 4 : 181-186 (1988)) ; specifically, the Genetools Computer Group (GCG) implementation of this algorithm, embodied in the program PEPTIDESTRUCTURE (Wisconsin Package v10.0, Genetics Computer Group (GCG), Madison, Wisc.). This method returns a measure of the probability that a given residue is found on the surface of the protein.

Regions where the antigenic index score is greater than 0.9 over at least 6 amino acids are indicated in Table 1A as "Predicted Epitopes", in particular embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the predicted epitopes described in Table 1A. It will be appreciated that depending on the analytical criteria used to predict antigenic determinants, the exact address of the determinant may vary slightly. Column 8, "Tissue Distribution" shows the expression profile of tissue, cells, and/or cell line libraries which express the polynucleotides of the invention. The first number in column 8 (preceding the colon), represents the tissue/cell source identifier code corresponding to the key provided in Table 4. Expression of these polynucleotides was not observed in the other tissues and/or cell libraries tested. For those identifier codes in which the first two letters are not "AR", the second number in column 8 (following the colon), represents the number of times a sequence corresponding to the reference polynucleotide sequence (e.g., SEQ ID NO : X) was identified in the tissue/cell source. Those tissue/cell source identifier codes in which the first two letters are "AR" designate information generated using DNA array technology. Utilizing this technology, cDNAs were amplified by PCR and then transferred, in duplicate, onto the array. Gene expression was assayed through hybridization of first strand cDNA probes to the DNA array. cDNA probes were generated from total RNA extracted from a variety of different tissues and cell lines. Probe synthesis was performed in the presence of 33P dCTP, using oligo (dT) to prime reverse transcription.

After hybridization, high stringency washing conditions were employed to remove non-specific hybrids from the array. The remaining signal, emanating from each gene target, was measured using a PhosphorImager. Gene expression was reported as Phosphor Stimulating Luminescence (PSL) which reflects the level of phosphor signal generated from the probe hybridized to each of the gene targets represented on the array. A local background signal subtraction was performed before the total signal generated from each array was used to normalize gene expression between the different hybridizations. The value presented after "[array code]:" represents the mean of the duplicate values, following background subtraction and probe normalization. One of skill in the art could routinely use this information to identify normal and/or diseased tissue (s) which show a predominant expression pattern of the corresponding polynucleotide of the invention or to identify polynucleotides which show predominant and/or specific tissue and/or cell expression. Column 9 provides the chromosomal location of polynucleotides corresponding to SEQ ID NO : X. Chromosomal location was determined by finding exact matches to EST and cDNA sequences contained in the NCBI (National Center for Biotechnology Information) UniGene database. Given a presumptive chromosomal location, disease locus association was determined by comparison with the Morbid Map, derived from Online Mendelian Inheritance in Man (Online Mendelian Inheritance in Man, OMIM). McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD) 2000. World Wide Web URL : <http://www.ncbi.nlm.nih.gov/omim/>. If the putative chromosomal location of the Query overlaps with the chromosomal location of a Morbid Map entry, an OMIM identification number is disclosed in column 10

labeled "OMIM Disease Reference (s)". A key to the OMIM reference identification numbers is provided in Table 5.

[27] Table 1B summarizes additional polynucleotides encompassed by the invention (including cDNA clones related to the sequences (Clone ID NO : Z), contig sequences (contig identifier (Contig ID :); contig nucleotide sequence identifiers (SEQ ID NO : X)), and genomic sequences (SEQ ID NO : B). The first column provides a unique clone identifier, "Clone ID NO : Z", for a cDNA clone related to each contig sequence. The second column provides the sequence identifier, "SEQ ID NO : X", for each contig sequence. The third column provides a unique contig identifier, "Contig ID : " for each contig sequence. The fourth column, provides a BAC identifier "BAC ID NO : A" for the BAC clone referenced in the corresponding row of the table. The fifth column provides the nucleotide sequence identifier, "SEQ ID NO : B" for a fragment of the BAC clone identified in column four of the corresponding row of the table.

The sixth column, "Exon From-To", provides the location (i. e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO : B which delineate certain polynucleotides of the invention that are also exemplary members of polynucleotide sequences that encode polypeptides of the invention (e. g., polypeptides containing amino acid sequences encoded by the polynucleotide sequences delineated in column six, and fragments and variants thereof).

[28] Table 2 summarizes homology and features of some of the polypeptides of the invention. The first column provides a unique clone identifier, "Clone ID NO : Z", corresponding to a cDNA clone disclosed in Table 1A. The second column provides the unique contig identifier, "Contig ID : " corresponding to contigs in Table 1A and allowing for correlation with the information in Table 1A. The third column provides the sequence identifier, "SEQ ID NO : X", for the contig polynucleotide sequence. The fourth column provides the analysis method by which the homology/identity disclosed in the Table was determined. Comparisons were made between polypeptides encoded by the polynucleotides of the invention and either a non-redundant protein database (herein referred to as "NR"), or a database of protein families (herein referred to as "PFAM") as further described below.

The fifth column provides a description of the PFAM/NR hit having a significant match to a polypeptide of the invention. Column six provides the accession number of the PFAM/NR hit disclosed in the fifth column. Column seven, "Score/Percent Identity", provides a quality score or the percent identity, of the hit disclosed in columns five and six. Columns 8 and 9, "NT From" and "NT To" respectively, delineate the polynucleotides in "SEQ ID NO : X" that encode a polypeptide having a significant match to the PFAM/NR database as disclosed in the fifth and sixth columns. In specific embodiments polypeptides of the invention comprise, or alternatively consist of, an amino acid sequence encoded by a polynucleotide in SEQ ID NO : X as delineated in columns 8 and 9, or fragments or variants thereof.

[29] Table 3 provides polynucleotide sequences that may be disclaimed according to certain embodiments of the invention. The first column provides a unique clone identifier, "Clone ID", for a cDNA clone related to contig sequences disclosed in Table 1A. The second column provides the sequence identifier, "SEQ ID NO : X", for contig sequences disclosed in Table 1A. The third column provides the unique contig identifier, "Contig ID : ", for contigs disclosed in Table 1A. The fourth column provides a unique integer 'a' where 'a' is any integer between 1 and the final nucleotide minus 15 of SEQ ID NO : X, and the fifth column provides a unique integer 'b' where 'b' is any integer between 15 and the final nucleotide of SEQ ID NO : X, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO : X, and where b is greater than or equal to a + 14. For each of the polynucleotides shown as SEQ ID NO : X, the uniquely defined integers can be substituted into the general formula of a-b, and used to describe polynucleotides which may be preferably excluded from the invention. In certain embodiments, preferably excluded from the invention are at least one, two, three, four, five, ten, or more of the polynucleotide sequence (s) having the accession number (s) disclosed in the sixth column of this Table (including for example, published sequence in connection with a particular BAC clone). In further embodiments, preferably excluded from the invention are the specific polynucleotide sequence (s) contained in the clones corresponding to at least one, two, three, four, five, ten, or more of the available material having the accession numbers identified in the sixth column of this Table (including for example, the actual sequence contained in an identified BAC clone).

[30] Table 4 provides a key to the tissue/cell source identifier code disclosed in Table 1A, column 8. Column 1 provides the tissue/cell source identifier code disclosed in Table 1A, Column 8. Columns 2-5 provide a description of the tissue or cell source. Codes corresponding to diseased tissues are indicated in column 6 with the word "disease". The use of the word "disease" in column 6 is non-limiting. The tissue or cell source may be specific (e. g. a neoplasm), or may be disease-associated (e. g., a tissue sample from a normal portion of a diseased organ). Furthermore, tissues and/or cells lacking the "disease" designation may still be derived from sources directly or indirectly involved in a disease state or disorder, and

therefore may have a further utility in that disease state or disorder. In numerous cases where the tissue/cell source is a library, column 7 identifies the vector used to generate the library.

[31] Table 5 provides a key to the OMIM reference identification numbers disclosed in Table 1A, column 10. OMIM reference identification numbers (Column 1) were derived from Online Mendelian Inheritance in Man (Online Mendelian Inheritance in Man, OMIM).

McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine, (Bethesda, MD) 2000. World Wide Web URL : <http://www.ncbi.nlm.nih.gov/omim/>.

Column 2 provides diseases associated with the cytologic band disclosed in Table 1A, column 9, as determined using the Morbid Map database.

[32] Table 6 summarizes ATCC Deposits, Deposit dates, and ATCC designation numbers of deposits made with the ATCC in connection with the present application.

[33] Table 7 shows the cDNA libraries sequenced, and ATCC designation numbers and vector information relating to these cDNA libraries.

[34] Table 8 provides a physical characterization of clones encompassed by the invention. The first column provides the unique clone identifier, "Clone ID NO : Z", for certain cDNA clones of the invention, as described in Table 1A. The second column provides the size of the cDNA insert contained in the corresponding cDNA clone.

Definitions [35] The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

[36] In the present invention, "isolated" refers to material removed from its original environment (e. g., the natural environment if it is naturally occurring), and thus is altered by the hand of man from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide. The term "isolated" does not refer to genomic or cDNA libraries, whole cell total or mRNA preparations, genomic DNA preparations (including those separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide/sequences of the present invention.

[37] As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence encoding SEQ ID NO : Y or a fragment or variant thereof ; a nucleic acid sequence contained in SEQ ID NO : X (as described in column 3 of Table 1A) or the complement thereof ; a cDNA sequence contained in Clone ID NO : Z (as described in column 2 of Table 1A and contained within a library deposited with the ATCC) ; a nucleotide sequence encoding the polypeptide encoded by a nucleotide sequence in SEQ ID NO : B as defined in column 6 of Table 1B or a fragment or variant thereof ; or a nucleotide coding sequence in SEQ ID NO : B as defined in column 6 of Table 1B or the complement thereof. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having an amino acid sequence encoded by a polynucleotide of the invention as broadly defined (obviously excluding poly-Phenylalanine or poly-Lysine peptide sequences which result from translation of a polyA tail of a sequence corresponding to a cDNA).

[38] In the present invention, "SEQ ID NO : X" was often generated by overlapping sequences contained in multiple clones (contig analysis). A representative clone containing all or most of the sequence for SEQ ID NO : X is deposited at Human Genome Sciences, Inc.

(HGS) in a catalogued and archived library. As shown, for example, in column 2 of Table 1A, each clone is identified by a

cDNA Clone ID (identifier generally referred to herein as Clone ID NO : Z). Each Clone ID is unique to an individual clone and the Clone ID is all the information needed to retrieve a given clone from the HGS library. Furthermore, certain clones disclosed in this application have been deposited with the ATCC on October 5, 2000, having the ATCC designation numbers PTA 2574 and PTA 2575 ; and on January 5, 2001, having the depositor reference numbers TS-1, TS-2, AC-1, and AC-2. In addition to the individual cDNA clone deposits, most of the cDNA libraries from which the clones were derived were deposited at the American Type Culture Collection (hereinafter "ATCC").

Table 7 provides a list of the deposited cDNA libraries. One can use the Clone ID NO : Z to determine the library source by reference to Tables 6 and 7. Table 7 lists the deposited cDNA libraries by name and links each library to an ATCC Deposit. Library names contain four characters, for example, "HTWE." The name of a cDNA clone (Clone ID) isolated from that library begins with the same four characters, for example, "HTWEP07". As mentioned below, Table 1A correlates the Clone ID names with SEQ ID NO : X. Thus, starting with an SEQ ID NO : X, one can use Tables 1, 6 and 7 to determine the corresponding Clone ID, which library it came from and which ATCC deposit the library is contained in. Furthermore, it is possible to retrieve a given cDNA clone from the source library by techniques known in the art and described elsewhere herein. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposits were made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for the purposes of patent procedure.

[39] In specific embodiments, the polynucleotides of the invention are at least 15, at least 30, at least 50, at least 100, at least 125, at least 500, or at least 1000 continuous nucleotides but are less than or equal to 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb, 7.5 kb, 5 kb, 2.5 kb, 2.0 kb, or 1 kb, in length. In a further embodiment, polynucleotides of the invention comprise a portion of the coding sequences, as disclosed herein, but do not comprise all or a portion of any intron. In another embodiment, the polynucleotides comprising coding sequences do not contain coding sequences of a genomic flanking gene (i. e., 5' or 3' to the gene of interest in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene (s).

[40] A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO : X, or the complement thereof (e. g., the complement of any one, two, three, four, or more of the polynucleotide fragments described herein), the polynucleotide sequence delineated in columns 8 and 9 of Table 2 or the complement thereof, and/or cDNA sequences contained in Clone ID NO : Z (e. g., the complement of any one, two, three, four, or more of the polynucleotide fragments, or the cDNA clone within the pool of cDNA clones deposited with the ATCC, described herein), and/or the polynucleotide sequence delineated in column 6 of Table 1B or the complement thereof. "Stringent hybridization conditions" refers to an overnight incubation at 42 degree C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM trisodium citrate), 50 mM sodium phosphate (pH 7. 6), 5x Denhardt's solution, 10% dextran sulfate, and 20 lg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0. 1x SSC at about 65 degree C.

[41] Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency) ; salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37 degree C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl ; 0. 2M NaH2PO4 ; 0. 02M EDTA, pH 7. 4), 0. 5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA ; followed by washes at 50 degree C with 1XSSPE, 0. 1% SDS.

In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e. g. 5X SSC).

[42] Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTING, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations.

The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due

to problems with compatibility.

[43] Of course, a polynucleotide which hybridizes only to polyA⁺ sequences (such as any 3' terminal polyA⁺ tract of a cDNA shown in the sequence listing), or to a complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide." Since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e. g., practically any double-stranded cDNA clone generated using oligo dT as a primer).

[44] The polynucleotide of the present invention can be composed of any polynucleotide or polydeoxynucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is a mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

[45] The polypeptide of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i. e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide. Including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslational natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer- RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination.

(See, for instance, PROTEINS-STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth. Enzymol. 182: 626-646 (1990); Rattan et al., Ann. N. Y. Acad. Sci. 663: 48-62 (1992)).

[46] "SEQ ID NO: X" refers to a polynucleotide sequence described, for example, in Tables 1A or 2, while "SEQ ID NO: Y" refers to a polypeptide sequence described in column 6 of Table 1A. SEQ ID NO: X is identified by an integer specified in column 4 of Table 1A.

The polypeptide sequence SEQ ID NO: Y is a translated open reading frame (ORF) encoded by polynucleotide SEQ ID NO: X. "Clone ID NO: Z" refers to a cDNA clone described in column 2 of Table 1A.

[47] "A polypeptide having functional activity" refers to a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein. Such functional activities include, but are not limited to: biological activity, antigenicity (ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody), immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

[48] The polypeptides of the invention can be assayed for functional activity (e. g. biological activity) using or routinely modifying assays known in the art, as well as assays described herein. Specifically, one of skill in the art may routinely assay signal transduction pathway component polypeptides (including fragments and variants) of the invention for activity using assays as described in Examples 38, 39, 49, 52-57, 64 and 67.

[49] "A polypeptide having biological activity" refers to a polypeptide exhibiting activity similar to, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i. e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention).

[50] Table 1A summarizes some of the polynucleotides encompassed by the invention (including contig sequences (SEQ ID NO : X) and clones (Clone ID NO : Z) and further summarizes certain characteristics of these polynucleotides and the polypeptides encoded thereby.

Polynucleotides and Polypeptides of the Invention
 TABLE 1A Gene Clone iD Contig SEQ ID ORF AA Predicted Epitopes Tissue Distribution Cytologic OMIM No: NO: Z ID: NO: X (From-To) SEQ Library code: count Band Disease ID (see Table IV for Reference(s); NO: Y Library Codes) 1 HDPTE21 1165861 11 33 - 1790 624 Pro-16 to Glu-22, AR051: 26, AR050: Arg-34 to Asn-41, 22, AR054: 21, AR089: Arg-49 to Lys-55, 1, AR061: 1 Leu-156 to Thr-163, H0529: 4, L0770: 4, Glu-169 to Gly-174, L0748: 4, L0749: 3, Ser-198 to Gly-214, L0777: 3, S0036: 2, Glu-246 to Pro-262, L0756: 2, S0360: 1, Arg-260 to Ser-271, H0036: 1, H0318: 1, Val-286 to Gly-291, H0457: 1, H0051: 1, Ser-304 to Gly-335, H0328: 1, H0688: 1, Pro-436 to Pro-451, S0002: 1, L0761: 1, Ser-482 to Gly-497, L0766: 1, L0804: 1, Val-498 to Ser-505, L0784: 1, H0521: 1 and Asp-564 to Lys-585, L0759: 1, 887711 443 1 - 639 1056 901381 444 570 - 112 1057 Gly-26 to Gly-32, 2 H6EDR51 1197894 12 1 - 1935 625 Glu-35 to Gln-44, AR089: 1, R061: 1 Arg-70 to Val-77, L0794: 11, L0777: 9, Ala-113 to Gly-123, H0255: 4, H0559: 4, Ser-128 to Phe-133, H0486: 3, H0581: 3, Gly-235 to His-242, L0869: 3, H0521: 3, Lys-249 to Leu-254, S0404: 3, H0556: 2, Pro-286 to Arg-292, H0580: 2, H0635: 2, Ser-309 to Glu-316, H0721: 2, H0135: 2, Lys-337 to Glu-360, H0703: 2, L0748: 2, Gln-366 to Gln-376, L0758: 2, H0543: 2, Glu-383 to Ala-388, H0422: 2, H0265: 1, Lys-391 to Leu-406, H0583: 1, H0656: 1, Gln-413 to Ala-420, H0638: 1, S0354: 1, Leu-430 to Leu-452, S0360: 1, H0637: 1, Lys-461 to Glu-467, H0600: 1, H0592: 1, Leu-476 to Lys-485, H0586: 1, H0587: 1, Lys0491 to Arg-496, H0257: 1, H0069: 1, Arg-500 to Gln-509, H0253: 1, S0049: 1, Ala-513 to Asp-539, H0199: 1, S0368: 1, Gln-544 to Ala-550, H0212: 1, H0494: 1, Glu-569 to Val-576, H0529: 1, L0763: 1, Arg-598 to Ser-620, L0637: 1, L0761: 1, Asn-622 to Ala-627, L0630: 1, L0764: 1, Ser-632 to Asn-645, L0648: 1, L0768: 1, L0766: 1, L0378: 1, L0806: 1, L0655: 1, L0657: 1, L0659: 1, L0769: 1, H0593: 1, H0670: 1, S0378: 1, S0152: 1, H0696: 1, H0134: 1, L0779: 1, H0445: 1, H0542: 1 and H0423: 1, 930798 445 1 - 1248 1058 Glu-26 to Gln-35, Arg-61 to Val-68, Ala-104 to Gly-114, Ser-19 to Phe-124, Gly-226 to His-233, Gly-240 to Leu-245, Pro-277 to Arg-283, 3 JARRA41 1154054 13 2 - 1276 626 Ser-5 to Arg-24 AR061: 3, AR089: 2 Trp-27 to Ala-32, L0777: 2, S0001: 1, Arg-48 to Gln-54, S0222: 1, H0575: 1, Lys-71 to Gln-79, H0618: 1, H0253: 1, Pro-93 to His-101, H0266: 1, H0038: 1, Lys-104 to Thr-110, H0616: 1, L0643: 1, Ser-119 to Gln-125, L0352: 1 and L0758: 1, Val-141 to Pro-152, Leu-158 to Gly-171, Asn-183 to Ala-198, Gly-217 to Asp-233, Ser-244 to Asn-258, Lys-264 to Leu-269, Ser-310 to Gly-316, Thr-326 to Glu-333, Ser-396 to Pro-403, Leu-416 to Lys-425, 926285 446 3 - 500 1059 Ser-3 to Arg-21, Trp-24 to Arg-29, Arg-45 to Gln-51, Lys-68 to Gln-76, Pro-90 to His-98, Lys-101 to Thr-107, Ser-116 to Gln-122, 4 HBXBI07 1171958 14 1 - 228 627 Ser-6 to Pro-14, AR061: 1, AR089: 1 954118 447 107 - 838 1060 5 HBXCM38 910686 15 402 - 1535 628 Val-36 to Glu-43, AR061: 2, AR090: 1 Lys-6 to Glu-71, L0439: 6, S0038: 3, L0803: 3, H0455: 2, L0769: 2, L0809: 2, L0741: 2, L0766: 2, S0624: 1, S0001: 1, H0663: 1, S0222: 1, H0441: 1, H0438: 1, H0036: 1, S0049: 1, L0769: 1, H0586: 1, H0024: 1, S0398: 1, S0051: 1, T0010: 1, H0059: 1, L0645: 1, L0774: 1, L0790: 1, L0663: 1, L0665: 1, H0345: 1, L0742: 1, L0748: 1, L0749: 1, H0707: 1, L0595: 1 and L0356: 1, 6 HCE3550 1227586 16 4 - 1650 629 Pro-1 to Ser-10, AR061: 1, AR089: 1 Pro-24 to Ser-29, H0521: 14, L0439: 6, Pro-43 to Glu-61, L0754: 6, L0794: 4, L0748: 4, S0278: 3, L0766: 3, L0751: 3, L0747: 3, L0749: 3, H0556: 2, H0486: 2, H0250: 2, H0179: 2, H0271: 2, S0002: 2, S0426: 2, L0770: 2, L0769: 2, L0775: 2, L0659: 2, L0411: 1, S0134: 1, H0638: 1, S0418: 1, S0420: 1, S0354: 1, S0358: 1, S0360: 1, S0222: 1, H0613: 1, H0052: 1, H0051: 1, L0143: 1, L0455: 1, H0124: 1, H0090: 1, H0551: 1, H0412: 1, S0038: 1, H0646: 1, S0344: 1, L0657: 1, L0772: 1, L0800: 1, L0662: 1, L0768: 1, L0804: 1, L0805: 1, L0790: 1, S0052: 1, H0593: 1, S0330: 1, H0539: 1, H0618: 1, S0332: 1, S0027: 1, L0741: 1, L0743: 1, L0740: 1, L0779: 1, L0731: 1, L0758: 1, H0445: 1, L0605: 1, S0196: 1 and H0423: 1, 961098 448 2 - 616 1061 7 HCEQD04 1150868 17 3 - 371 630 His-1 to Cys-13, AR061: 5, AR089: 4 Glu-31 to Ala-49, H0052: 2 Asp-82 to Pro-86, 927873 449 1 - 364 1062 Glu-2 to Cys-11, Glu-29 to Ala-47, Asp-80 to Pro-86, 8 HDPH192 909900 18 366 - 1346 631 Asn-1 to Gly-6, AR089: 7, AR061: 3 Pro-34 to Arg-43, H0521: 7, L0766: 5, Lys-51 to Ile-56, H0318: 3, L0655: 3, Lys-58 to Arg-63, H0522: 3, H0543: 3, Tyr-73 to Gly-85, H0657: 2, H0553: 2, Ala-98 to Ala-

104, L0632; 2, L0748; 2, Ser-115 to Asp-124, H0445; 2, L0605; 2, Gly-189 to Gly-194, H04422; 2, H0265; 1, Pro-1999 to Leu-204, H0556; 1, S0114; 1, Ala-214 to Asp-225, H0583; 1, H0650; 1, Thr-260 to Gln-268, S0116; 1, H0341; 1, Pro-279 to Ser-284, S0360; 1, H0676; 1, H0497; 1, H0486; 1, H0075; 1, H0581; 1, H0421; 1, S0398; 1, H0271; 1, H0031; 1, H0090; 1, H0591; 1, H0058; 1, L0938; 1, L0667; 1, L0363; 1, L0774; 1, L0775; 1, L0658; 1, L0659; 1, L0809; 1, L0647; 1, L0790; 1, H0701; 1, H0658; 1, H0555; 1, L0779; 1, L0777; 1, L0731; 1 and H0423; 1, 9 HDPLT89 952403 19 83 - 931 632 Lys-13 to Gly-28, AR054; 57, AR051; Arg-64 to Gly-71, 36, AR050; 36, AR069; Pro-131 to Glu-137, 4, AR061; 1, Gln-152 to Asp-159, L0731; 18, L0766; 16, Lys-170 to Gly-179, H0521; 1, L0745; 7, Thr-183 to Trp-185, L0754; 7, L0806; 6, Arg-193 to Glu-206, L0749; 6, L0794; 5, Asp-222 to Val-228, L0666; 5, S0360; 4, Ser-262 to Ser-277, L0663; 4, L0740; 4, L0747; 4, H0655; 3, L0771; 3, L0662; 3, L0774; 3, L0665; 3, L0439; 3, L0777; 3, L0758; 3, H0638; 2, H0431; 2, H0620; 2, H0494; 2, S0002; 2, L0769; 2, L0803; 2, L0438; 2, H0689; 2, H0659; 2, H0658; 2, H0518; 2, S0206; 2, L0750; 2, S0242; 2, H0423; 2, H0650; 1, H0341; 1, H0661; 1, H0662; 1, H0300; 1, S0418; 1, S0376; 1, H0580; 1, S0045; 1, L0717; 1, H0453; 1, H0370; 1, H0497; 1, H0574; 1, H0632; 1, H0486; 1, L0021; 1, S0474; 1, H0544; 1, H0046; 1, H0050; 1, H0510; 1, H0594; 1, S0340; 1, S0003; 1, T0023; 1, H0553; 1, H0644; 1, H0674; 1, H0040; 1, H102; 1, H0641; 1, H0538; 1, L0763; 1, L0648; 1, L0768; 1, L0387; 1, L0804; 1, L0775; 1, L0805; 1, L0655; 1, L0783; 1, L0788; 1, S0374; 1, H0691; 1, H0435; 1, H0670; 1, H0648; 1, H0522; 1, H0134; 1, S014; 1, L0779; 1, L0597; 1, S0026; 1, H0542; 1, H0543; 1, H0506; 1 and H0352; 1, 10 HDPSU48 1228284 20 466-987 633 Gln-1 to Gly-8, AR089; 1, AR061; 0, Ile-15 to Asp-20, L0766; 10, L0803; 6, Lys-61 to Glu-59, L0754; 5, S0152; 4, Pro-93 to Lys-102, L0771; 3, L0656; 2, Ala-147 to Leu-156, L0662; 2, L0774; 2, Pro-159 to Asp-174, S0380; 2, H0423; 2, H0624; 1, H0685; 1, L0002; 1, H0583; 1, L0760; 1, H0661; 1, S0358; 1, S0360; 1, H0637; 1, H0601; 1, H0486; 1, H0457; 1, H0247; 1, S0003; 1, T0067; 1, S0002; 1, S0426; 1, H0529; 1, L0770; 1, L0764; 1, L0806; 1, L0655; 1, L0659; 1, L0666; 1, L0663; 1, L0664; 1, S0428; 1, S0126; 1, H0435; 1, H0521; 1, H0522; 1, L0747; 1, L0756; 1, L0759; 1, H0445; 1 and H0422; 1, 909949 450 227-976 1063 Ser-9 to Arg-14, Arg-48 to Arg-54, Gln-71 to Lys-77, Ile-91 to Asp-96, Lys-137 to Glu-145, Pro-169 to Lys-178, Ala-223 to Leu-232, Pro-235 to Asp-250, 11 HDPEW80 909918 21 94-765 634 Asp-8 to Cys-21, H0521; 9, L0595; 2, Val-25 to Asn-33, L0593; 1 and L0594; 1, Thr-47 to Pro-55, Ala-62 to Thr-68, Val-79 to Lys-88, Asn-91 to Asn-104, Tyr-114 to Gly-120, Thr-157 to Gly-182, Ile-217 to Thr-224, 12 HDQFY84 1092137 22 2-276 635 Glu-94 to Tyr-102, AR051; 2, AR050; 1, Pro-105 to Asn-112, AR061; 1, AR054; 1, Thr121 to Gly-137, AR089; 0, Glu-157 to Gly-162, S0354; 8, H0254; 2, Glu-179 to Phe-186, S0358; 2, H0580; 2, Cys-211 to Thr-222, H0521; 2, L0656; 1, Ser-240 to Lys-245, H0590; 1, H0457; 1, Thr-262 to Asn-279, H0271; 1 and H0488; 1, Arg-288 to Pro-306, Asn-332 to Gln-339, Ser-375 to Leu-382, Arg-408 to Gly-415, Asp-423 to Thr-428, Ser-471 to Asn-476, Pro-545 to Gly-551, Ser-605 to Pro-616, Ala-662 to Gly-667, Thr-675 to Tyr-682, Glu-714 to Trp-720, Pro-722 to Val-732, Pro-787 to Thr-795, Arg-811 to Glu-816, Gln-830 to Thr-891, 971615 451 506-1567 1064 13 HEONQ19 930705 23 3-806 636 Ala-13 to Arg-29, AR089; 2, AR061; 0, Gln-35 to Lys-48, H0457; 9, L0596; 3, L0803; 2, H0673; 1, L0455; 1, L0359; 1, L0764; 1, L0389; 1, L0375; 1, L0655; 1, L0809; 1, L0790; 1 and L0752; 1, 14 HFCB556 910073 24 209-565 637 AR061; 1, AR069; 1, H0009; 1, 15 HFKKZ94 1163070 25 3-719 636 Arg-15 to Trp-20, AR061; 4, AR089; 2, Asn-26 to Trp-34, S0278; 4, H0581; 4, Lys-115 to Glu-125, L0751; 4, H0620; 3, Glu-154 to Trp-163, L0764; 3, L0662; 3, Ser-192 to Val-197, L0659; 3, L0439; 3, Gly-216 to Arg-222, L0754; 3, H0542; 3, H0170; 2, H0402; 2, H0580; 2, H0550; 2, H0333; 2, H0012; 2,
 T0010; 2, H0252; 2,
 H0063; 2, H0059; 2,
 S0002; 2, L0775; 2,
 L0655; 2, L0663; 2,
 L0665; 2, H0593; 2,
 H0658; 2, H0539; 2,
 H0555; 2, L0743; 2,
 L0744; 2, L0752; 2,
 L0731; 2, L0543; 2,
 T0024; 1, H0265; 1,
 H0650; 1, H0656; 1,
 S0212; 1,
 H0306; 1,
 S0305; 1, S0360; 1,
 S0046; 1, H0619; 1,
 S0222; 1, S0014; 1,
 H0613; 1, H0492; 1,
 H0250; 1, H0635; 1,
 H0427; 1, L0021; 1,
 H0038; 1, H0421; 1,
 H0399; 1, H0416; 1,
 H0188; 1, S0250; 1,
 L0143; 1, H0617; 1,
 H0673; 1, H0124; 1,
 H0163; 1, H0634; 1,
 H0087; 1, T0067; 1, H0264; 1, H0272; 1, H0412; 1, H0413; 1, H0100; 1, S0344; 1, S0426; 1, L0770; 1, L0638; 1, L0761; 1, L0794; 1, L0650; 1, L0661; 1, L0546; 1, S0053; 1, H0689; 1, H0521; 1, S0314; 1, L0748; 1, L0740; 1, L0779; 1, L0780; 1, L0753; 1, L0759; 1, H0445; 1, H0595; 1, L0362; 1, H0653; 1 and H0506; 1, 926486 452 1-720 1065 Arg-16 to Trp-21, Asn-27 to Pro-35, Lys-116 to Glu-126, Gly-155 to Trp-164, Ser-193 to Val-198, Gly-217 to Arg-223, 16 HHBGJ53 1187668 26 312-1 639 AR089; 8, AR061; 5, L0740; 2 and H0373; 1, 909912 453 1-282 1066 Ser-1 to Ser-7, Ser-25 to Arg-31, 1, 17 HHFJF24 1212624 27 1374-538 640 Lys-1 to Ala-6, AR089; 1, AR061; 0, Ser-38 to Gln-43, S0001; 1, H0619; 1, H0586; 1, H0427; 1 and L0595; 1, 910065 454 3-206 1067 18 HHFMM10 1178901 28 369-751 641 Ser-19 to Thr-29, AR089; 20, AR061; 1, Gly-62 to Arg-64, H0063; 1, H0619; 1, Gln-102 to Phe-113, and S0036; 1, 962997 455 95-493 1068 Gly-1 to Ser-13, Ile-24 to Phe-29, 19 HHPPBA42 901921 29 1-912 642 Gly-9 to Gln-15, AR061; 133, AR089; 118, L0764; 4, L0659; 4, L0761; 3, S0360; 2, H0031; 2, L0662; 2, L0747; 2, L0760; 2, H0624; 2, L0295; 1, S0356; 1, S0132; 1, H0351; 1, L0394; 1, L0738; 1, H0051; 1, H0328; 1, L0796; 1, L0646; 1, L0800; 1, L0794; 1, L0549; 1, L0803; 1, L0806; 1, L0809; 1, L0788; 1, L0789; 1, S0374; 1, H0435; 1, H0539; 1, S0378; 1, S0146; 1, L0754; 1, L0780; 1, L0752; 1 and L0591; 1, 20 HHPSF99 1217052 30 2-916 643 Gly-1 to Ile-11, AR089; 1, AR061; 0, Pro-49 to Asp-59, H0038; 3, H0616; 3, Val-64 to Leu-70, S0386; 2, L0366; 2, Gly-105 to Ser-112, S0001; 1, S0360; 1, Ser-130 to Ala-146, H0208; 1, S0046; 1, Asn-223 to Val-229, S0206; 1, H0486; 1, Asn-272 to Asp-278, H0052; 1, H0201; 1, Lys-294 to Tyr-305, T0010; 1, S0036; 1, L0776; 1, S0216; 1, H0701; 1, H0593; 1, S0152; 1, H0521; 1, L0753; 1, L0758; 1 and S0031; 1, 910024 456 1-906 1069 Pro-49 to Asp-56, Val-61 to Leu-67, Gly-102 to Ser-109, Ser-127 to Ala-143, Asn-220 to Val-226, 21 HKABX13 1167182 31 1-786 644 Lys-49 to Trp-55, AR089; 12, AR061; 2 Tyr-66

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414 HHSD185 942246 424 2 - 502 1037 Ser-12 to Gln-25, AR061: 3, AR089: 2 Pro-29 to Phe-39, S0007: 3, S0001: 1, Gly-81 to Gly-89, H0618: 1, H0009: 1, Glu-143 to Trp-155, S0051: 1, L0763: 1, L0439: 1 and L0758: 1, 951168 622 356 - 42 1235 Arg-82 to Trp-88, 415 HTJMD31 942848 425 1 - 462 1038 Pro-17 to Asn-23, AR089: 14, AR061: 6 S0300: 2, L0439: 2, H0438: 1, H0618: 1, H0502: 1, H0616: 1, H0468: 1, L0772: 1, L0806: 1, L0384: 1, L0666: 1, L0758: 1 and H0423: 1, 416 HWAOD57 943039 426 2 - 1009 1039 Asp-2 to Pro-7, AR089: 1, AR061: 0 Leu-18 to Arg-27, H0255: 2, H0486: 1, Glu-52 to Ser-59, H0581: 1, H0529: 1 and Pro-90 to Pro-97, H0543: 1, Pro-116 to Glu-121, 417 HLWAO5 944904 427 356 - 1351 1040 Ala-1 to Arg-9, AR061: 2, AR089: 1 Leu-11 to Pro-18, H0586: 5, L0751: 2, H0170: 1, H0638: 1, H0553: 1, H0477: 1, S0002: 1, H0529: 1, L0766: 1, L0803: 1, H0672: 1 and H0543: 1, 418 HDPC164 945527 428 25 - 1047 Arg-9 to Arg-18, AR069: 2, AR061: 1 Leu-107 to Gln-113, H0521: 4, L0803: 3, Asp-126 to Thr-131, S0358: 2, H0489: 2, H0046: 2, L0794: 2, L0686: 2, H0144: 2, S0126: 2, S0342: 1, H0663: 1, S0356: 1, H0013: 1, L0021: 1, H0705: 1, H0150: 1, H0268: 1, H0039: 1, H0622: 1, H0038: 1, H0551: 1, S0422: 1, L0598: 1, L0646: 1, L0766: 1, L0653: 1, L0656: 1, L0789: 1, L0532: 1, L0663: 1, H0558: 1, L0748: 1, L0759: 1, S0434: 1, L0596: 1 and H0506: 1, 419 HBXDJ07 946830 429 125 - 652 1042 Glu-62 to Lys-68, AR061: 2, AR089: 2 Asn-105 to Gly-113, L0439: 11, L0794: 5, L0686: 5, S0222: 4, H0052: 3, L0756: 3, H0624: 2, S0628: 2, S0038: 2, L0638: 2, L0805: 2, L0644: 2, L0438: 2, L0740: 2, H0171: 1, S6024: 1, H0013: 1, H0374: 1, H0050: 1, S0050: 1, S0386: 1, L0769: 1, L0768: 1, L0776: 1, L0659: 1, L0789: 1, H0144: 1, L0745: 1 and H0746: 1, 420 HAMFD12 952438 430 3 - 539 1043 Thr-41 to Leu-52, AR089: 3, AR061: 1 Leu-64 to Cys-72, H0271: 10, H0052: 8, Pro-92 to Arg-98, H0556: 7, L0439: 7, Ser-110 to Gly-116, L0754: 7, H0622: 6, L0778: 5, L0769: 4, H0265: 3, H0295: 3, H0580: 3, S0222: 3, H0013: 3, H0156: 3, H0051: 3, H0494: 3, L0659: 3, S0358: 2, H0208: 2, S6014: 2, H0135: 2, H0634: 2, S0002: 2, S0426: 2, L0770: 2, L0796: 2, L0373: 2, L0803: 2, L0375: 2, L0655: 2, L0666: 2, L0438: 2, H0672: 2, H0521: 2, L0747: 2, L0750: 2, L0756: 2, L0588: 2, H0542: 2, H0543: 2, H0170: 1, S0212: 1, S0282: 1, S0300: 1, H0305: 1, H0589: 1, L0619: 1, H0619: 1, S6026: 1, H0050: 1, H0370: 1, H0600: 1, H0592: 1, H0468: 1, T0040: 1, H0635: 1, H0002: 1, S0010: 1, H0390: 1, H0581: 1, H0421: 1, H0085: 1, T0110: 1, H0041: 1, N0006: 1, H0050: 1, H0012: 1, H0620: 1, T0003: 1, H0024: 1, H0687: 1, H0252: 1, H0604: 1, H0031: 1, H0644: 1, H0628: 1, H0598: 1, H0087: 1, H0264: 1, S0112: 1, T0041: 1, H0560: 1, S0150: 1, H0529: 1, L0640: 1, L0761: 1, L0643: 1, L0808: 1, L0658: 1, L0809: 1, L0514: 1, L0789: 1, L0663: 1, L0644: 1, L0665: 1, S0428: 1, S0053: 1, H0144: 1, H0690: 1, H0518: 1, H0696: 1, H0438: 1, H0576: 1, S0392: 1, L0740: 1, L0731: 1, L0759: 1, S0031: 1, L0596: 1, S0011: 1, H0667: 1 and S0192: 1, 421 HFKH40 952470 431 641 - 1756 1044 Gly-16 to His-25, AR089: 1, AR061: 0 H0457: 7, H0521: 2, H0586: 1, H0458: 1, S0278: 1, H0069: 1, H0820: 1, H0179: 1, H0271: 1, H0416: 1, S0144: 1, H0703: 1, H0593: 1 and H0522: 1, 422 HDTA108 953265 432 316 - 567 1045 Leu-13 to Val-25, AP061: 1, AR089: 1 His-32 to Arg-32, H0521: 4, H0580: 2, H0583: 1, H0486: 1, H0625: 1, S0466: 1, L0666: 1, S0242: 1, H0542: 1 and H0543: 1, 423 HMKCX80 956254 433 194 - 616 1046 Gln-7 to Asp-19, AR089: 7, AR061: 3 Leu-34 to Ser-42, H0392: 1, H0427: 1, H0318: 1, L0663: 1, H0345: 1 and L0596: 1, 424 HCEMF99 951308 434 2 - 637 1047 AR061: 1, AR089: 1 S0136: 3, L0779: 3, H0171: 1, H0052: 1, H0038: 1, L0766: 1, H0547: 1, S0031: 1 and S0242: 1, 425 HWLHF10 963422 435 115 - 978 1048 Ile-44 to Gln-50, AR089: 26, AR061: 4 S03454: 1, H0661: 1 and L0603: 1, 426 HMEG82 963855 436 2 - 991 1049 Asp-1 to Pro-12, AR061: 49, AR089: 19 427 HFXDR37 969519 437 1485 - 556 1050 Glu-18 to Thr-23, AR061: 2, AR089: 1 L0766: 2, S0001: 1, H0592: 1, H0575: 1, H0644: 1, H0039: 1 and H0144: 1, 428 HNNAS46 969470 438 1 - 834 1051 AR089: 1, AR061: 0 H0638: 2, H0521: 2, L0752: 2, H0677: 2, H0650: 1, H0484: 1, H0458: 1, H0580: 1, H0586: 1, H0575: 1, H0081: 1, S0036: 1, H0063: 1, H0560: 1, L0809: 1, S0126: 1, S0328: 1, L0744: 1, L0740: 1, L07454: 1 and H0543: 1, 429 HRAAS26 971219 439 17 - 536 1052 Glu-25 to Arg-31, AR054: 23, AR050: Glu-71 to His-76, 18 AR051: 12, AR061: Leu-85 to Leu-92, 12, AR089: 8 Gly-129 to Ser-143, L0803: 7, L0794: 4, L0748: 4, L0591: 4, L0770: 3, L0804: 3, S0142: 2, L0789: 2, L0743: 2, L0747: 2, L0749: 2, L0752: 2, S0360: 1, S0046: 1, H0548: 1, H0309: 1, H0327: 1, H0012: 1, L0769: 1, L0773: 1, L0767: 1, L0774: 1, L0775: 1, L0776: 1, L0790: 1, L0791: 1, H0435: 1, H0660: 1, H0648: 1, H0521: 1, H0555: 1, L0750: 1, L0779: 1, L0777: 1, L0775: 1, L0758: 1 and S0434: 1, 430 HHEEL28 973096 440 1 - 378 1053 AR089: 1, AR061: 0 L0766: 7, H0486: 4, L0794: 4, H0520: 4, L0754: 4, L0777: 4,
 L0755: 4, L0599: 4, L0779: 3,
 L0803: 3, L0779: 3,
 H0542: 3, H0624: 2,
 S0418: 2, S0360: 2,
 H0551: 2, L0770: 2,
 L0662: 2, L0558: 2,
 L0665: 2, H0144: 2,
 H0547: 2, H0519: 2,
 H0522: 2, L0756: 2,
 L0755: 2, L0858: 2,
 H0170: 1, H0556: 1,
 H0567: 1, H0580: 1,
 L0717: 1, S0222: 1,
 H0574: 1, H0599: 1,
 S0474: 1, H0544: 1,
 H0266: 1, H0252: 1,
 T0023: 1, H0553: 1,
 T0042: 1, S0422: 1,
 L0369: 1, L0763: 1,
 L0761: 1, L0772: 1,
 L0521: 1, L0387: 1,
 L0650: 1, L0806: 1,
 L0653: 1, L0655: 1,
 L0789: 1, L0790: 1,
 L0663: 1, S0063: 1, S0374: 1, H0435: 1, H0670: 1, H0651: 1, H0521: 1, H0436: 1, H0345: 1, L0439: 1, L0745: 1, L0749: 1, L0750: 1, L0759: 1, L0485: 1, L0593: 1, S0026: 1, H0665: 1, H0543: 1, H0423: 1, H0422: 1 and S0458: 1, 431 HCET22 973324 441 112 - 1863 1054 Asn-1 to Gly-9, AR061: 11, AR089: 4 Gln-30 to Gly-35, L0741: 8, L0766: 7, L0794: 6, H0306: 4, H0052: 4, L0768: 3, L0603: 3, H0542: 3, S0360: 2, H0457: 2, H0617: 2, H0606: 2, S0036: 2, H0100: 2, L0800: 2, H0672: 2, H0436: 2, L0777: 2, H0543: 2, H0650: 2, L0785: 1, H0341: 1, H0254: 1, H0402: 1, S0420: 1, H0580: 1, S0045: 1, H0645: 1, H0550: 1, S0222: 1, S6014: 1, H0592: 1, N0009: 1, S0280: 1, H0599: 1, H0618: 1, S0182: 1, H581: 1, S0049: 1, H0194: 1, N0007: 1, H0271: 1, H0252: 1, H0063: 1, H0468: 1, H0412: 1, H0079: 1, T0041: 1, H0646: 1, S0144: 1, L0763: 1, L0770: 1, L0769: 1, L0761: 1, L0372: 1, L07646: 1, L0645: 1, L0764: 1, L0774: 1, L0792: 1, L0666: 1, L0665: 1, H0519: 1, H0435: 1, H0539: 1, H0518: 1, L0747: 1, L0755: 1, H0653: 1, H0136: 1, H0677: 1 and S0446: 1, 432 HCMSF59 912284 442 657 - 361 1055 AR089: 2,

AR061: 2, L0604: 16, S0366: 9, L0485: 7, L0622: 6, L0623: 6, H0599: 6, H0373: 6, H0196: 4, L0163: 4, L0777: 4, L0520: 3, H0002: 2, S0364: 2, S0330: 2, L0747: 2, H0171: 1, H0549: 1, H0486: 1, H0013: 1, H0253: 1, H0318: 1, S0049: 1, H0251: 1, L0471: 1, S0051: 1, H0616: 1, S0038: 1, H0100: 1, H0561: 1, L0803: 1, L0782: 1, L0809: 1, L0779: 1, L0759: 1, and L0584: 1, 975280 623 52 - 705 1236 His-10 to Gly-16, Pro-65 to Ala-70, Ala-86 to Lys-101.

[51] The first column in Table 1A provides the gene number in the application corresponding to the clone identifier. The second column in Table 1A provides a unique "Clone ID NO : Z" for a cDNA clone related to each contig sequence disclosed in Table 1A.

This clone ID references the cDNA clone which contains at least the 5' most sequence of the assembled contig and at least a portion of SEQ ID NO : X was determined by directly sequencing the referenced clone. The reference clone may have more sequence than described in the sequence listing or the clone may have less. In the vast majority of cases, however, the clone is believed to encode a full-length polypeptide, in the case where a clone is not full-length, a full-length cDNA can be obtained by methods described elsewhere herein.

[52] The third column in Table 1A provides a unique "Contig ID" identification for each contig sequence. The fourth column provides the "SEQ ID NO : X" identifier for each of the contig polynucleotide sequences disclosed in Table 1A. The fifth column, "ORF (From- To)", provides the location (i. e., nucleotide position numbers) within the polynucleotide sequence "SEQ ID NO : X" that delineate the preferred open reading frame (ORF) shown in the sequence listing and referenced in Table 1A, column 6, as SEQ ID NO : Y. Where the nucleotide position number "To" is lower than the nucleotide position number "From", the preferred ORF is the reverse complement of the referenced polynucleotide sequence.

[53] The sixth column in Table 1A provides the corresponding SEQ ID NO : Y for the polypeptide sequence encoded by the preferred ORF delineated in column 5. In one embodiment, the invention provides an amino acid sequence comprising, or alternatively consisting of, a polypeptide encoded by the portion of SEQ ID NO : X delineated by "ORF (From-To)". Also provided are polynucleotides encoding such amino acid sequences and the complementary strand thereto.

[54] Column 7 in Table 1A lists residues comprising epitopes contained in the polypeptides encoded by the preferred ORF (SEQ ID NO : Y), as predicted using the algorithm of Jameson and Wolf, (1988) Comp. Appl. Biosci. 4 : 181-186. The Jameson-Wolf antigenic analysis was performed using the computer program PROTEAN (Version 3. 11 for the Power Macintosh, DNASTAR, Inc., 1228 South Park Street Madison, WI). In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, at least one, two, three, four, five or more of the predicted epitopes as described in Table 1A. It will be appreciated that depending on the analytical criteria used to predict antigenic determinants, the exact address of the determinant may vary slightly.

[55] Column 8 in Table 1A provides an expression profile and library code : count for each of the contig sequences (SEQ ID NO : X) disclosed in Table 1A, which can routinely be combined with the information provided in Table 4 and used to determine the tissues, cells, and/or cell line libraries which predominantly express the polynucleotides of the invention.

The first number in column 8 (preceding the colon), represents the tissue/cell source identifier code corresponding to the code and description provided in Table 4. For those identifier codes in which the first two letters are not "AR", the second number in column 8 (following the colon) represents the number of times a sequence corresponding to the reference polynucleotide sequence was identified in the tissue/cell source. Those tissue/cell source identifier codes in which the first two letters are "AR" designate information generated using DNA array technology. Utilizing this technology, cDNAs were amplified by PCR and then transferred, in duplicate, onto the array. Gene expression was assayed through hybridization of first strand cDNA probes to the DNA array. cDNA probes were generated from total RNA extracted from a variety of different tissues and cell lines. Probe synthesis was performed in the presence of 33P dCTP, using oligo (dT) to prime reverse transcription.

After hybridization, high stringency washing conditions were employed to remove non-specific hybrids from the array. The remaining signal, emanating from each gene target, was measured using a Phosphorimager. Gene expression was reported as Phosphor Stimulating Luminescence (PSL) which reflects the level of phosphor signal generated from the

probe hybridized to each of the gene targets represented on the array. A local background signal subtraction was performed before the total signal generated from each array was used to normalize gene expression between the different hybridizations. The value presented after "[array code]:" represents the mean of the duplicate values, following background subtraction and probe normalization. One of skill in the art could routinely use this information to identify normal and/or diseased tissue (s) which show a predominant expression pattern of the corresponding polynucleotide of the invention or to identify polynucleotides which show predominant and/or specific tissue and/or cell expression.

[56] Column 9 in Table 1A provides a chromosomal map location for certain polynucleotides of the invention. Chromosomal location was determined by finding exact matches to EST and cDNA sequences contained in the NCBI (National Center for Biotechnology Information) UniGene database. Each sequence in the UniGene database is assigned to a "cluster"; all of the ESTs, cDNAs, and STSs in a cluster are believed to be derived from a single gene. Chromosomal mapping data is often available for one or more sequence (s) in a UniGene cluster; this data (if consistent) is then applied to the cluster as a whole. Thus, it is possible to infer the chromosomal location of a new polynucleotide sequence by determining its identity with a mapped UniGene cluster.

[57] A modified version of the computer program BLASTN (Altschul et al., J. Mol.

Biol. 215 : 403-410 (1990) ; and Gish and States, Nat. Genet. 3 : 266-272 (1993)) was used to search the UniGene database for EST or cDNA sequences that contain exact or near-exact matches to a polynucleotide sequence of the invention (the "Query"). A sequence from the UniGene database (the "Subject") was said to be an exact match if it contained a segment of 50 nucleotides in length such that 48 of those nucleotides were in the same order as found in the Query sequence. If all of the matches that met this criteria were in the same UniGene cluster, and mapping data was available for this cluster, it is indicated in Table 1A under the heading "Cytologic Band". Where a cluster had been further localized to a distinct cytologic band, that band is disclosed ; where no banding information was available, but the gene had been localized to a single chromosome, the chromosome is disclosed.

[58] Once a presumptive chromosomal location was determined for a polynucleotide of the invention, an associated disease locus was identified by comparison with a database of diseases which have been experimentally associated with genetic loci. The database used was the Morbid Map, derived from OMIMTM (supra). If the putative chromosomal location of a polynucleotide of the invention (Query sequence) was associated with a disease in the Morbid Map database, an OMIM reference identification number was noted in column 10, Table 1A, labelled "OMIM Disease Reference (s)". Table 5 is a key to the OMIM reference identification numbers (column 1), and provides a description of the associated disease in Column 2.

TABLE IB Clone ID SEQ ID CONTIG BAC ID : A SEQ ID EXON NO : Z NO : X ID : NO : 8 From-To HFCBB56 24 910073
AC068296 1268 1-225 HIBBF63 75 912715 AC009065 1269 1-70 850-1112 1169-1822 1707-1779 1874-1924 2836-2908
3006-4160 HIBBF63 75 912715 AC012171 1270 1-64 159-209 1122-1194 1292-1527 1593-2446 HIBBF63 75 912715
AC005346 1271 1-70 874-1136 1193-1646 1731-1803 1898-1948 2861-2933 3031-4185 HIBBF63 75 912715 AC009065
1272 1-547 HIBBF63 75 912715 AC012171 1273 1-547 HIBBF63 75 912715 AC009065 1274 1-424 HIBBF63 75 912715
AC005346 1275 1-547 HIBBF63 75 912715 AC012171 1276 1-419 HIBBF63 75 912715 AC005346 1277 1-424
H2CBH45 90 963811 AC068243 1278 1-267 1540-1640 3095-3380 3393-3556 3901-3967 4137-4639 5287-5856 5916-
6588 7029-7876 8324-8414 H2CBH45 90 963811 AC068243 1279. 1-309 HBGQT03 93 908173 AC024045 1280 1-218
457-549 660-819 2039-2238 2529-2763 2876-3033 3631-3810 3941-4058 4184-4322 4727-4851 5161-6181 HBGQT03
93 908173 AC024045 1281 1-176 HBGQT03 93 908173 AC024045 1282 1-461 960-1030 1194-1959 2041-2516 3037-
3122 3398-3455 4055-4366 4547-4599 4967-5216 5321-5461 6521-7174 7564-7841 8311-8758 8829-8969 8997-10118
10257-10910 12058-12385 12438-12953 13729-13873 HCEPH71 97 522739 AL365319 1283 1-484 HCEPH71 97
522739 AL360715 1284 1-494 HCOOZ11 100 965306 AL022238 1285 1-121 839-983 1445-1513 2156-3430 3550-3763
3859-3972 4449-4595 4960-5152 5385-5529 5744-5972 6327-7067 7097-7152 7210-8073 8079-8680 8772-11399
12956-13317 13736-14155 14311-14753 16294-16357 16648-16806 16874-17059 17685-17787 HCOOZ11 100965308
AL022238 1286 1-540 HCOOZ11 100 965306 AL022238 1287 1-655 HCWFF88 101 506577 AC025670 1288 1-300
HCWFF88 101 506577 AL157951 1289 1-624 HCWFF88 101 506577 AL157951 1290 1-409 HCWFF88 101 506577
AL157951 1291 1-83 HDPFF24 104 909232 AC020910 1292 1-353 359-468 787-861 1877-2199 4963-5089 5342-5440
6133-6734 9933-10319 HDPFF24 104 909232 AC020910 1293 1-814 HDPFF24 104 909232 AC020910 1294 1-437
HDTKQ14 107 886936 AL359542 1295 1-140 1249-4264 HDTKQ14 107 886936 AL023953 1296 1-140 1249-4264
HDTKQ14 107 886936 AL359542 1297 1-499 HDTKQ14 107 886936 AL359542 1298 1-145 HDTKQ14 107 886936
AL023953 1299 1-499 HFTDF15 113 857020 AL355277 1300 1-406 HFTDF15 113 857020 AC024511 1301 1-406

HFTDF15 113 657020 AL365277 1302 1-430 HFTDF15 113 657020 AC024511 1303 1-430 HFTDF15 113 657020
 AL365277 1304 1-526 HFTDF15 113 657020 AC024511 1305 1-526 HLQDT35 117 839777 AC010998 1306 1-44 640-
 884 1203-1261 1994-2178 2303-2474 2991-3088 3592-3757 4262-4364 4742-5802 6235-7057 7126-8472 HLQDT35 117
 839777 AC013357 1307 1-44 504-884 1203-1261 1994-2178 2303-2474 2991-3088 3592-3757 4262-4364 4742-5802
 6235-7057 7126-8472 HLQDT35 117 839777 AC010998 1308 1-768 HLQDT35 117 839777 AC013357 1309 1-6035
 8430-11057 HLQDT35 117 839777 AC010998 1310 1-278 HLQDT35 117 839777 AC013357 1311 1-278 HLWFN63 118
 908437 AC006599 1312 1-30 1525-1711 5426-5502 7038-7273 7590-7735 8960-9048 11665-11800 12889-13194 13907-
 14119 14889-15043 15926-16164 18759-19079 20581-20693 22531-22783 23817-24956 26153-26283 26791-27141
 28145-29220 HLWFN63 118 908437 AL303378 1313 1-30 1525-1711 5426-5502 7038-7273 7590-7735 11665-11800
 12889-13194 13907-14119 14889-15043 15926-16164 18759-19079 20581-20693 22531-22753 23817-24956 26153-
 26283 26791-27141 28145-29220 HLWFN63 118 908437 AC006599 1314 1-2939 HLWFN63 118 908437 AL303378
 1315 1-2939 HMSCD15 120 918133 AC027008 1316 1-1190 HMSCD15 120 918133 AL158207 1317 1-130 923-1252
 1765-3269 4138-4483 6546-7734 HMSCD15 120 918133 AL158207 1318 1-371 HPMFL08 128 959569 23016 1319 1-
 477 HPMFL08 128 959569 23016 1320 1-650 HTEAG49 135 954614 AL390796 1321 1-1310 HTEAG49 135 954614
 AL357045 1322 1-1310 HTEAG49 135 954614 AL390796 1323 1-627 HTEAG49 135 954614 AL357045 1324 1-627
 HTLBH67 136 751985 AC008439 1325 1-62 293-400 452-976 1016-1058 1463-1534 1886-2026 2110-2249 2401-2463
 3324-4027 4192-4288 4694-5330 5485-5650 5813-6282 6273-6401 6475-6559 6728-6847 6979-7205 7573-7678 7730-
 8146 8334-8866 8885-9392 HTLBH67 136 751985 AC008781 1326 1-85 254-371 505-731 1098-1201 1255-1671 1718-
 2387 2408-2915 3113-3244 3382-4278 4504-4538 4650-5645 HTLBH67 136 751985 AC022420 1327 1-62 295-403 458-
 979 1019-1061 1466-1537 1890-2030 2114-2253 2405-2467 3328-4030 4195-4291 4697-5333 5488-5653 5816-6265
 6276-6404 6478-6562 6731-6850 6982-7208 7575-7678 7732-8148 8195-8864 8885-9392 9580-9721 9859-10754
 10980-11014 11128-12121 HTLBH67 136 751985 AC005368 1328 1-64 294-399 451-975 1015-1057 1462-1533 1885-
 2025 2109-2248 2400-2462 3323-4028 4191-4287 4693-5329 5484-5649 5812-6264 6275-6403 6477-6561 6730-6849
 6981-7207 7575-7678 7732-8148 8201-8866 8887-9394 9582-9723 9861-10759 10985-11019 11131-12126 HTLBH67
 136 751985 AC007871 1329 1-292 HTLBH67 136 751985 AC022420 1330 1-323 1372-1431 1657-1821 2377-2485
 4488-4700 4954-5061 6224-6547 6819-6965 7268-7333 8086-8593 9697-10068 10109-10623 10645-10680 10812-
 10871 10982-11123 11345-11383 11877 12000 12310 13467 HTLBH67 136 751985 AC022420 1331 1-1292 HTLBH67
 136 751985 AC005368 1332 1-292 HTLJC71 137 922923 AC009516 1333 1-2009 HTLJC71 137 922923 AC007957 1334
 1-1747 HTLJC71 137 922923 AC018751 1335 1-2009 HTLJC71 137 922923 AC023490 1336 1-2009 HTLJC71 137
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The sixth column, "Exon From-To", provides the location (i. e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO : B which delineate certain polynucleotides of the invention that are also exemplary members of polynucleotide sequences that encode polypeptides of the invention (e. g., polypeptides containing amino acid sequences encoded by the polynucleotide sequences delineated in column six, and fragments and variants thereof).

http://www.wipo.int/pctdb/en/fetch.jsp?SEARCH_IA=US2001001312&DBSELECT=PCT... 6/16/2008

(DBL5 BIG 23% 512 613 SISTER) (MCF2 TRANSFORMING SEQUENCE-LIKE PROTEIN). HHFJF24 910065 454
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98% 3 158 NUCLEOTIDE T EXCHANGE FACTOR DBS (DBL5 BIG SISTER) 1 (FRAGMENT). HHFM10 1178901 28
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domain PF00169 50.5 406 621 2.1.1 blastx.2 p116Rip [Mus musculus] gb#AA818198.1# 76% 1 624 HPIA101 1078178
40blastx.14 unnamed protein product gi#4756912#emb#CAB 36% 213 437 [unidentified] 42323.1# 42% 414 476 72% 183
215 HPIA101 909928 466 HMMER PFAM: PH domain PF00169 30.3 294 482 2.1.1 blastx.2 unnamed protein product
emb#CAB42187.1# 62% 10 195 [unidentified] HPJCT50 919636 467 HMMER PFAM: PH domain PF00169 61.4 728 1015
2.1.1 blastx.2 (AF210918) SWAP-70 gb#AAF24486.1#AF2 85% 98 1453 [Homo sapiens] 10818.1 HPMFE91 1164740 42
blastx.14 (AF136450) goodpasture gi#4835935#gb#AAD3 89% 20 1129 antigen-binding protein 0288.1#AF136450-1
97% 1097 1813 [Homo sapiens] HPMFE91 910026 468 HMMER PFAM: PH domain PF00169 81.9 332 613 2.1.1 blastx.2
(AF136450) goodpasture gb#AAD30288.1#AF1 94% 263 955 antigen-binding protein 35450-1 [Homo sapiens]
HRAED51 1090522 43 blastx.14 iacGAP [Dictyostellium gi#2190355#emb#CAA 40% 363 569 discoidium] 71241.1# 48%
195 305 HRAED51 909859 469 HMMER PFAM: RhoGAP domain PF00520 78.3 259 504 2.1.1 blastx.2 beta-chimaerin
[Rattus gb#AAA40809.1# 26% 259 585 norvegicus] HSMBA19 924885 470 HMMER PFAM: PH domain PF00169 34.3
289 528 2.1.1 blastx.2 (AL096767) cu579N16.2 emb#CAB63063.1# 49% 4 531 (SET binding factor) 1 76% 533 807
[Homo sapiens] HSYCY88 914775 45 HMMER PFAM: PH domain PF00169 34 811 966 2.1.1 blastx.2 putative [Rattus
emb#CAA62297.1# 97% 607 966 norvegicus] 63% 21 437 88% 425 532 50% 992 1111 44% 1041 1136 HTEDW26
909749 48 HMMER PFAM: FYVE zinc finger PF01363 88.9 321 521 2.1.1 blastx.2 (AF093839) actin-5g#Sg#CAAC27698.1#
89% 57 959 filament binding protein 51 1 81 Frabin [Rattus norvegicus] HTEKD92 1050346 47 blastx.14 (AK000074)
unnamed gi#7019925#dbj#BAA9 87% 482 1165 protein product [Homo 0927.1# sapiens] HTEKD92 910027 471 HMMER
PFAM: PH domain PF00169 51.4 252 530 2.1.1 blastx.2 (AK000074) unnamed dbj#BAA90927.1# 87% 486 1151 protein
product [Homo sapiens] HTLDT05 909752 472 HMMER PFAM: PH domain PF00169 36.9 59 271 2.1.1 blastx.2
(AK000004) FLJ00004 dbj#BAA92229.1# 77% 47 487 protein [Homo sapiens] HTPDS90 529764 473 HMMER PFAM: PH
domain PF00169 65.3 132 440 2.1.1 blastx.2 putative [Rattus emb#CAA52297.1# 79% 75 458 norvegicus] 65% 2 58
HTPHM71 1194698 50 blastx.14 CDNA FLJ20260 FIS, spr#BAA91043#BAA9 62% 61 348 CLONE COLF7627. 1043 70%
1423 1659 42% 520 675 59% 1192 1287 47% 700 762 23% 889 1002 42% 1054 1131 80% 808 837 27% 1552 1671 38%
600 653 HTPHM71 909878 474 HMMER PFAM: PH (pleckstrin PF00169 38.8 57 341 1.8 homology) domain blastx.2
(AK000267) unnamed dbj#BAA91043.1# 53% 5 341 protein product [Homo 31% 71 929 sapiens] 65% 1139 1207 32%
550 690 42% 857 1034 HUJAR12 944393 475 HMMER PFAM: PH domain PF00169 63.5 69 359 2.1.1 blastx.2
(AB080430) CDEP dbj#BAA24267.1# 45% 3 677 [Homo sapiens] HWAGP22 1150195 52 blastx.14 (AL031027)
gi#3292902#emb#CAA 55% 1653 1021 prediction:(method:"ge 19842.1# nfinder"). 1 1 1 PROTEIN". sp HWAGF22
909919 476 HMMER PFAM: FYVE zinc finger PF01363 89.9 516 716 2.1.1 blastx.2 (AL031027) emb#CAA19842.1# 50%
78 710 prediction:(method:"ge nfinder"). 1 1 1 PROTEIN". sp HWACE37 906968 53 HMMER PFAM: PH (pleckstrin
PF00169 60.73 39 353 1.8 homology) domain blastx.2 brain beta spectrin [Mus gb#AAC420401.1# 30% 93 386 musculus]
HWLFB60 1223499 54 blastx.14 CG1513 PROTEIN. spr#Q9V5D4#Q9V5D4 64% 1445 1924 72% 1127 1459 66% 2 355
33% 1943 2218 52% 518 580 24% 1295 1393 38% 89 142 HWLFB60 910018 477 HMMER PFAM: PH domain PF00169
43 8 241 2.1.1 blastx.2 (AF000195) Contains gb#AAC24270.14 63% 14 241 similarity to Pfam domain: PF00169 (PH). 1
HDQFS16 909833 478 HMMER PFAM: Protein kinase C PF00433 57.51 287 445 1.8 terminal domain blastx.2
(AJ245709) Akt-3 protein emb#CAB53537.1# 100% 236 460 [Homo sapiens] 100% 3 116 HDQVDS99 937850 56 HMMER

407.1.8 (contains ATP/GTP binding P-loop) blaxt.2 small GTP-binding gb#AAC51194.2# 97% 3 407 protein Rab27b [Homo sapiens] HRAACA1 1162856 79 blaxt.14 rab4b [Canis familiaris] gi#919#emb#CAA3980 100% 54 677 0.1# HRAACA51 912776 499 HMMER PFAM: Ras family PF00071 310.6 56 666 2.1.1 blaxt.2 rab4b [Canis familiaris] emb#CAA3980.1# 100% 43 666 HSHAV32 912812 500 HMMER PFAM: Ras family PF0071 242.77 192 872 1.8 (contains ATP/GTP binding P-loop) blaxt.2 AB034244) RAB23 db#BAA87324.1# 99% 162 872 protein [Homo sapiens] HTPDE66 971281 81 HMMER PFAM: Ras family PF00071 73.52 260 427 1.8 (contains ATP/GTP binding P-loop) blaxt.2 small GTP-binding gb#AAA31261.1# 100% 260 427 protein [Cryptotagus 63% 216 281 cuniculus] HTPDV73 997659 82 blaxt.14 N-methyl-D-aspartate gb#286238#db#BAA02 66% 39 74 receptor subunit [Rattus 500.1# 30% 123 182 rattus] 70% 5 34 71% 290 310 83% 123 140 85% 248 268 71% 331 351 HTPDV73 912947 501 HMMER PFAM: Ras family PF00071 205.32 306 740 1.8 (contains ATP/GTP binding P-loop) blaxt.2 (AL049685) hypothetical emb#CAB41256.1# 97% 312 746 protein [Homo sapiens] HTPHE33 963658 502 HMMER PFAM: Ras family PF00071 94.19 993 1433 1.8 (contains ATP/GTP binding P-loop) blaxt.2 (AF095350) RAB-like gb#AAD51377.1# AF0 63% 993 1478 protein 2A [Homo 95350-1 93% 793 1014 sapiens] HUFDN58 1224809 84 blaxt.14 RAS-LIKE PROTEIN sp#P03967#RASD-DI 47% 664 921 RASD CDI 57% 490 672 (TRANSFORMING 53% 937 981 PROTEIN P23), HUFDN58 912929 503 HMMER PFAM: Ras family PF00071 80.7 42 296 2.1.1 blaxt.2 ras-related protein emb#CAA78508.1# 43% 3 299 [Dicyotestellum dicoelum] HUVFX92 1225329 85 blaxt.14 GTP-binding protein ypt1 pir#S30096#S30096 88% 54 308 [similarity] - Neurospora caassa HUVFX92 912672 504 HMMER PFAM: Ras family PF00071 161 81 278 2.1.1 blaxt.2 (AF101310) similar to ga#AAC69218.1# 100% 54 275 RAS-related proteins; contains similarity 1 HWAEG71 1128232 86 blaxt.14 rab-related GTP-binding gi#206543#gb#AAA42 96% 85 690 protein [Rattus 00.1# norvegicus] HWAEG71 931547 505 HMMER PFAM: Ras family PF00071 147.95 116 475 1.8 (contains ATP/GTP binding P-loop) blaxt.2 rab-related GTP-binding gb#AAA42000.1# 99% 86 493 protein [Rattus 80% 477 569 norvegicus] HWAHD49 1228064 87 blaxt.14 GTP-BINDING sp#Q9X571#Q9X571 97% 391 747 PROTEIN RAH 94% 742 1011 9FRAGMENT), HWAHD49 972413 506 HMMER PFAM: Ras family PF00071 143.42 394 717 1.8 (contains ATP/GTP binding P-loop) blaxt.2 LMW G protein-low gb#AAB2869.1# 95% 391 720 molecular-weight GTP-76% 726 764 binding protein [mice, HT4 neural cell line, peptide, 208 aa] [Mus sp.] HWLG31 1178225 88 blaxt.14 RAB15 [Rattus gi#206537#gb#AAA41 92% 81 716 norvegicus] 995.1# HWLG31 912581 507 HMMER PFAM: Ras family PF00071 301.8 98 562 2.1.1 blaxt.2 RAB15 [Rattus gb#AAA41995.1# 90% 71 562 norvegicus] HWLKF25 912842 508 HMMER PFAM: Ras family PF00071 298.2 311 889 2.1.1 blaxt.2 (AB036693) RAB-like gb#BAA89542.1# 100% 287 889 protein [Homo sapiens] H2CBH45 963811 90 HMMER PFAM: Src homology PF00018 134 310 1.8 domain 3 blaxt.2 Kryn [Mus musculus] db#BA19686.1# 85% 2 373 79% 381 467 87% 460 483 70% 131 160 HAGDN53 895963 509 HMMER PFAM: Src homology PF00018 22.95 270 335 1.8 domain 3 blaxt.2 coded for by C. elegans gb#AAA96115.1# 43% 1765 455 cDNA yk34a9.5; coded 38% 103 156 for by C. elegans 1 elegans] HAMFM39 971347 92 HMMER PFAM: Src homology PF00018 67.14 1136 1306 1.8 domain 3 blaxt.2 (AK001509) unnamed db#GAA91729.1# 59% 4511 4017 protein product [Homo sapiens] HBGQT03 908173 93 HMMER PFAM: SH3 domain PF00018 66.5 615 785 2.1.1 blaxt.2 (AF130979) SH3 domain gb#AAG04472.1# AF1 93% 3 791 containing protein 9511 30979-1 [Homo sapiens] HBG5J13 1150790 94 blaxt.14 ferrienterobactin receptor gi#1778500#gb#AAB4 63% 729 1 precursor [Escherichia 0783.1# coli] HBG5J13 878322 510 HMMER PFAM: Src homology PF00018 4.07 445 510 1.8 domain 3 blaxt.2 ferrienterobactin receptor gb#AAB40783.1# 92% 64 684 precursor [Escherichia coli] HBIB089 908782 95 HMMER PFAM: SH3 domain PF00018 49.7 212 376 2.1.1 blaxt.2 p115 [Homo sapiens] emb#CAA55394.1# 41% 14 397 HCECM90 945088 96 HMMER PFAM: Src homology PF00018 53.06 392 568 1.8 domain 3 HCEPH71 522739 97 HMMER PFAM: Src homology PF00018 4.22 33 62 1.8 domain 3 HCFMT57 1175204 98 blaxt.14 (AF039571) peripheral gi#4104812#gb#AAD1 96% 45 629 benzodiazepine receptor 1957.1# 74% 702 887 interacting protein; PBR- 100% 887 979 IP/PRAX1 [Homo 52% 381 500 sapiens] 44% 381 461 55% 327 386 28% 161 319 50% 74 803 58% 780 830 35% 160 243 34% 1693 1770 47% 468 518 55% 190 243 58% 795 830 42% 622 684 29% 73 153 42% 607 663 35% 54 137 36% 643 717 31% 631 717 25% 136 231 38% 111 188 28% 114 230 28% 144 227 HCFMT57 765375 511 HMMER PFAM: Src homology PF00018 14.55 107 3 1.8 domain 3 blaxt.2 (AF039571) peripheral gb#AAD11957.1# 96% 377 3 benzodiazepine receptor interacting protein; PBR- IP/PRAX1 [Homo sapiens] HCOMAM05 1173146 99 blaxt.14 epidermal growth factor gi#530822#gb#AAA62 44% 456 712 receptor kinase substrate 280.1# 59% 189 371 [Homo sapiens] 46% 723 851 23% 54 293 36% 126 191 63% 108 111 113 HCOMM05 925952 512 HMMER PFAM: Src homology PF00018 59.48 178 342 1.8 domain 3 blaxt.2 epidermal growth factor gb#AAA62280.1# 46% 445 840 receptor kinase substrate 43% 115 435 [Homo sapiens] 23% 43 222 HCOOZ1 1 965306 100 HMMER PFAM: Src homology PF00018 5.22 179 214 1.8 domain 3 blaxt.2 (AL022238) d1J042K10.2 emb#CAA18266.1# 100% 182 589 (supported by GENSCAN, FGENSE and GENWISE) HGWFF68 506577 101 HMMER PFAM: Src homology PF00018 4.92 140 181 1.8 domain 3 HDMAV01 911386 513 HMMER PFAM: Src homology PF00018 52.13 264 413 1.8 domain 3 blaxt.2 unnamed protein product emb#CAB42388.1 73% 111 410 [unidentified] 100% 3 116 HDPA47 929193 103 HMMER PFAM: Src homology PF00018 12.52 691 810 1.8 domain 3 blaxt.2 (AL049683) hypothetical emb#CAB41255.1# 69% 145 1026 protein [Homo sapiens] 53% 945 1022 HDPPF 24 909232 104 HMMER PFAM: KRAB box PF 01352 121 159 349 2.1.1 blaxt.2 (AC007228) R31665-2 gb#AAD23606.1# AC0 50% 158 457 [AA 1- 673] [Homo 07228-1 sapiens] HDPPQ35 966248 105 HMMER PFAM: Src

homology PF00018 14.07 600 749 1.8 domain 3 blastx.2 (AL049683) hypothetical emb#CAB41255.1# 39% 84 1148 protein [Homo sapiens] HDPSR74 911396 106 HMMER PFAM: Src homology PF00018 47,19 293 460 1.8 domain 3 blastx.2 (AF104246) enhancer of gbb#AAD11795.1# 48% 281 553 filamentation 1 homology [Gallus gallus] HDTKO14 868936 107 HMMER PFAM: Src homology PF00018 12.87 430 546 1.8 domain 3 blastx.2 (AL049683) hypothetical emb#CAB41255.1# 100% 439 555 protein [Homo sapiens] 56% 76 291 HE6GF02 1150897 109 blastx.14 (AJ007012) Fish protein g#3702174#emb#CAA 75% 795 613 [Mus musculus] 07416.1# 66% 603 427 70% 89 70 39% 603 430 40% 604 613 38% 792 637 39% 795 637 41% 600 427 38% 582 433 37% 552 481 37% 150 70 50% 532 485 54% 459 427 HE6GF02 911263 514 HMMER PFAM: Src homology PF00018 51.15 10 174 1.8 domain 3 blastx.2 (AJ007012) Fish protein emb#CAA07416.14 77% 10 186 [Mus musculus] 44% 201 276 HE6PK12 905884 109 HMMER PFAM: Src homology PF00018 58.12 197 381 1.8 domain 3 blastx.2 (AF136380) SH3P12 gb#AAD27647.1#AF1 82% 59 367 protein [Homo sapiens] 36380 1 HE9SE62 911476 110 HMMER PFAM: Src homology PF00018 47.65 268 435 1.8 domain 3 blastx.2 (AK000007) FLJ00007 db#BAA92232.1# 43% 4 435 protein [Homo sapiens] 64% 877 927 HEQPL36 968826 515 HMMER PFAM: Src homology PF00018 79.81 316 483 1.8 domain 3 blastx.2 (AL049758) dJ437M21.3 emb#CAB51395.1# 93% 178 486 (protein kinase C and casein kinase substrate in neurons 2) [Homo sapiens] HFBDJ13 911264 112 HMMER PFAM: SH3 domain PF00018 78.6 105 269 2.1.1 blastx.2 (AF030131) Plenty of gb#AAC40070.1# 78% 3 473 SH3s: POSH [Mus musculus] HFTDF15 657020 113 HMMER PFAM: Src homology PF00018 4.85 168 203 1.8 domain 3 HHFCOK09 965304 115 HMMER PFAM: TBC domain PF00566 179.1 2305 1655 2.1.1 blastx.2 (AL022238) dJ1042K10.0 emb#CAA18266.1# 97% 2635 1268 (supported by 98% 1276 389 GENSCAN, FGENSE and GENWISE) [Homo sapiens] HSDS562 935932 116 HMMER PFAM: RhoGEF domain PF00621 51.3 229 486 2.1.1 blastx.2 (AJ250425) Collyblatin 1 emb#CAB65968.1# 96% 1 483 [Rattus norvegicus] HLQDT35 839777 117 HMMER PFAM: Src homology PF00018 3.85 342 419 1.8 domain 3 blastx.2 (AK000579) unnamed db#BAA91266.1# 98% 252 458 protein product [Homo sapiens] HLWFN63 908437 118 HMMER PFAM: Src homology PF00018 12.81 515 664 1.8 domain 3 blastx.2 (AL049683) hypothetical emb#CAB41255.1# 44% 464 1024 protein [Homo sapiens] HMEFT66 856149 119 HMMER PFAM: Src homology PF00018 28.51 5 136 1.8 domain 3 HMSCD1 519133 120 HMMER PFAM: Src homology PF00018 41.06 453 599 1.8 domain 3 blastx.2 (AK000975) unnamed db#BAA91451.1# 98% 453 635 protein product [Homo sapiens] 387 479 sapiens] 28% 80 175 HSMH064 746582 121 HMMER PFAM: Src homology PF00018 11.08 316 405 1.8 domain 3 blastx.2 (AF030131) Plenty of gb#AAC40070.1# 47% 1 411 SH3s: POSH [Mus musculus] HMTAW83 911385 122 HMMER PFAM: Src homology PF00018 76.18 1 159 1.8 domain 3 blastx.2 (AF230904) c-Cbl-gb#AAF37854.1#AF2 94% 1 354 Interacting protein [Homo sapiens] 30904-1 52% 7 210 sapiens] 48% 7 169 61% 298 351 75% 425 460 HMVAM09 963814 128 HMMER PFAM: Src homology PF00018 4.79 728 802 1.8 domain 3 blastx.2 (AK001580) unnamed db#BAA1769.1# 96% 20 602 protein product [Homo sapiens] HNSAA28 946988 124 HMMER PFAM: SH3 domain PF00018 149 757 915 2.1.1 blastx.2 (AF146277) adapter gb#AAD34565.1#AF1 82% 4 1554 protein CMS [Homo 46277-1 sapiens] HNSAA28 972348 516 blastx.14 (AF146277) adapter gb#A4960047#gb#AAD3 88% 21 449 protein CMS [Homo 4595.1 sapiens] HAF146277-1 sapiens] HCGEQ43 935465 517 HMMER PFAM: Src homology PF00018 28.13 58 132 1.8 domain 3 blastx.2 (AF132480) Esee2 protein gb#AAD19748.1# 93% 37 132 [Mus musculus] HOUDH19 1150918 126 blastx.14 (AC007842) BC331191-1 gb#5080758#gb#AAD3 91% 350 27 [Homo sapiens] 9268.1#AC007842-3 HOUDH19 908588 518 HMMER PFAM: KRAB box PF01352 169.7 241 429 2.1.1 blastx.2 (AC007842) BC331191-1 gb#AAD39268.1#AC0 91% 228 549 [Homo sapiens] 07842-3 HOUPF36 911293 137 HMMER PFAM: PDZ domain PF00595 35.3 322 558 2.1.1 (Also known as DHR or GLGF). blastx.2 (AF162130) MAGUK gb#AAD45919.2#AF1 91% 196 646 protein TEM-61 [Homo 62130-1 98% 23 193 sapiens] HPMFL08 959569 128 HMMER PFAM: Src homology PF00018 4.97 209 238 1.8 domain 3 HRSMO49 723025 129 HMMER PFAM: Src homology PF00018 4.76 199 270 1.8 domain 3 HSDI69 917180 130 HMMER PFAM: SH3 domain PF00018 4.09 362 429 1.8 domain 3 HSDSB06 949151 131 HMMER PFAM: SH3 domain PF00018 249.3 483 647 2.1.1 blastx.2 (AL133047) hypothetical emb#CAB61374.1# 98% 3 863 protein [Homo sapiens] 30% 6 848 33% 222 848 HSFAM09 573345 519 HMMER PFAM: Src homology PF00018 5.33 198 218 1.8 domain 3 HSSAX53 507509 133 HMMER PFAM: Src homology PF00018 4.36 266 331 1.8 domain 3 HSSAV49 689674 520 HMMER PFAM: Src homology PF00018 36.33 77 169 1.8 domain 3 blastx.2 (AF146277) adapter gb#AAD34565.1#AF1 97% 65 166 protein CMS [Homo 46277-1 sapiens] HTEAG49 954614 135 HMMER PFAM: Src homology PF00018 4.51 312 238 1.8 domain 3 HTLBH67 751985 136 HMMER PFAM: Src homology PF00018 37.78 16 162 1.8 domain 3 HTLJCT7 922923 137 HMMER PFAM: Src homology PF00018 9.14 1152 1340 1.8 domain 3 blastx.2 (AL133030) hypothetical emb#CAB61362.1# 94% 3 1355 protein [Homo sapiens] HTPAD46 503313 138 HMMER PFAM: Src homology PF00018 4.14 160 186 1.8 domain 3 HTTKP07 911390 139 HMMER PFAM: Src homology PF00018 15.62 47 196 1.8 domain 3 blastx.2 (AL049683) hypothetical emb#CAB41255.1# 51% 8 289 protein [Homo sapiens] 58% 292 450 HUCOGW17 933557 140 HMMER PFAM: Src homology PF00018 20.28 647 739 1.8 domain 3 blastx.2 Grai protein [Homo emb#CAA71414.2# 67% 1 261 sapiens] 50% 608 751 83% 756 809 40% 187 246 HWHGF52 726102 141 HMMER PFAM: Src homology PF00018 5.01 325 387 1.8 domain 3 blastx.2 Dbs=Dbl guanine gb#BAA33461.1# 74% 3 203 nucleotide exchange 72% 319 417 factor homolog [mice, 73% 203 259 321 1 HWHIB69 690442 521 HMMER PFAM: Src homology PF00018 31.65 91 255 1.8 domain 3 blastx.2 (AF178432) SH3 protein gb#AAF35985.1#AF1 70% 91 315

[Homo sapiens] 78432 1 100% 303 329 HWLFH94 1151387 143 blastx.14 (AK000265) unnamed gi#7020230<db>BAA9 41% 545 345 protein product [Homo 1041.1# 53% 689 594 sapiens] 52% 949 887 HWLFH94 009662 522 HMMER PFAM: Src homology PF00018 58.42 308 463 1.8 domain 3 blastx.2 (AK000265) unnamed db|BAA91041.1# 40% 215 535 protein product [Homo sapiens] HMMBM13 909683 144 HMMER PFAM: Src homology PF00018 59.84 126 281 1.8 domain 3 blastx.2 Eps8 [Mps8 [Mus musculus] gb|AAA16358.1# 35% 33 317 37% 324 527 HWWND34 911357 145 HMMER PFAM: Src homology PF00018 14.09 686 853 1.8 domain 3 blastx.2 (AF053130) gb|AAAC40124.1# 42% 56 874 unconventional myosin 66% 768 868 MYO15 [Mus musculus] HCCEML27 771667 523 HMMER PFAM: Src homology PF00017 42.63 14 202 1.8 domain 2 blastx.2 (AL049924) hypothetical emb|CAB43206.1# 88% 2 322 protein [Homo sapiens] HELHJ69 1128924 147 blastx.14 (AF124251) SH2- gi#4704739<gb>AAD2 81% 66 593 containing protein Nsp3 5246.1#AF124251~1 76% 586 624 [Homo sapiens] 52% 590 640 60% 55 99 63% 612 644 HELHJ69 911262 524 HMMER PFAM: Src homology PF00017 72.59 241 483 1.8 domain 2 blastx.2 (AF124251) SH2- gb|AAD28246.1#AF1 78% 67 645 containing protein Nsp3 24251~1 76% 587 625 [Homo sapiens] 60% 56 100 HFKA09 952634 525 HMMER PFAM: Src homology PF00017 46.9 758 1036 2.1.1 domain 2 HSBFB79 965764 149 HMMER PFAM: Src homology PF00017 69.47 384 614 1.8 domain 2 HSLKA77 911589 525 HMMER PFAM: Src homology PF00017 37.25 301 405 1.8 domain 2 blastx.2 tensin [Gallus gallus] gb|AAA49087.1 58% 178 432 51% 29 115 31% 3 155 hagr21 1090433 151 blastx.14 p66shc [Homo sapiens] gi#1899055<gb>AAB4 69% 848 1150 9972.1# 72% 134 412 59% 380 475 37% 665 751 35% 72 164 34% 701 778 hagr21 1002124 527 blastx.14 MUS p66 Shc [Mus gi#1200456<gb>AAA9 91% 62 258 [musculus] 1777.1# HHFNH27 1025277 152 blastx.2 collagen alpha 1(II) chain pir#S05272<CG>HU7L 30% 89 1609 precursor - human 28% 53 1606 30% 1061 1741 32% 1094 1606 32% 956 1741 32% 1094 1606 31% 851 1735 30% 830 1741 30% 1073 1618 28% 1094 1831 28% 1022 1735 30% 1088 1741 30% 21 593 30% 89 655 34% 86 910 28% 18 593 27% 27 455 32% 128 655 30% 80 601 34% 27 257 30% 42 599 28% 53 541 34% 21 257 28% 33 455 35% 12 257 33% 9 269 28% 36 593 36% 21 245 28% 21 386 30% 9 593 27% 67 477 30% 37 477 29% 1746 289 31% 1656 835 32% 1848 952 29% 1662 955 36% 525 55 37% 525 19 32% 525 37 33% 1859 1063 30% 1656 1021 30% 1644 958 32% 642 64 34% 534 85 33% 592 11 30% 654 7 30% 226 8 28% 596 2 30% 648 85 41% 229 11 30% 599 17 37% 211 11 34% 226 23 33% 250 11 35% 226 23 43% 190 11 36% 259 41 44% 125 45 52% 128 72 HTLT105 1217625 153 blastx.14 CDNA FLJ10243 FIS, sp|BAA91565<BAA9 49% 213 584 CLONE: 1505 HEMBB1000631, WEAKLY SIMILAR TO 1 HTLT105 1095161 528 blastx.14 (AK001105) UNNAMED gi#7022161<db>BaaA9 49% 212 577 protein product [Homo 1505.1# sapiens] HAPNV33 151374 154 blastx.14 (AK001267) unnamed gi#7022415<db>BAA9 100% 1 774 protein product [Homo 1590.1# sapiens] HAPNV33 947872 529 HMMER PFAM: ATPases PF00004 120.31 61 450 1.8 associated with various cellular activities (AAA) blastx.14 (AF016427) Contains gi#2291232<gb>AAB6 53% 1 447 similarity to Piam 5351.1# domain: 1 elegans] HBTAEB4 1128800 155 blastx.14 ATP-dependent Clp gi#1651401<db>BAA9 100% 3 299 protease ATP-binding 5601.1# subunit ClpA, [Escherichia coli] HBTAEB4 781945 533 HMMER PFAM: ATPases PF00004 20.81 122 232 1.8 associated with various cellular activities (AAA) HDPVY89 827026 156 HMMER PFAM: ATPases PF00004 30.6 431 490 2.0 1.1 associated with various cellular activities (AAA) HGLDB21 455474 531 HMMER PFAM: ATPases PF00004 19.89 12 80 1.8 associated with various cellular activities (AAA) HMAN37 947881 156 HMMER PFAM: ATPases PF00004 109 436 642 2.1.1 associated with various cellular activities (AAA) blastx.2 Similarity to Yeast MSP1 emb|CVA493516.1# 45% 91 642 protein (TAT-binding homolog 4) (SW:MSP1-YEAST) [Caenorhabditis elegans] HODAK55 745532 532 HMMER PFAM: ATPases PF00004 60.69 11 157 1.8 associated with various cellular activities (AAA) HSLIE159 1128801 160 blastx.14 ATP-dependent Clp gi#1651401<db>BaaA9 94% 3 770 protease ATP-binding 5601.1# subunit ClpA, [Escherichia coli] HSLIE159 781945 533 HMMER PFAM: ATPases PF00004 20.14 96 206 1.8 associated with various cellular activities (AAA) HSQFH29 1217061 161 blastx.14 SPAF, sp|Q922K7<Q922K7 89% 101 1723 52% 5 208 36% 854 961 HSQFH29 967708 534 HMMER PFAM: ATPases PF00004 97.36 193 393 1.8 associated with various cellular activities (AAA) blastx.14 (AF049099) SPAF [Mus gi#1405619<gb>AAD0 83% 70 417 musculus] 2481.1# 43% 76 414 76% 408 470 61% 3 41 HTLEA35 1107230 162 blastx.14 (AK001571) unnamed gi#7022907<db>BaaA9 100% 3 479 protein product [Homo 1764.1# sapiens] HTLEA35 627028 535 HMMER PFAM: ATPases PF00004 19.08 12 260 1.8 associated with various cellular activities (AAA) HUVG63 969432 536 HMMER PFAM: ATPases PF00004 332.15 621 1178 1.8 associated with various cellular activities (AAA) blastx.14 (AF159063) SKD1- gi#5732691<gb>AAD4 97% 138 1448 homolog [Homo sapiens] 9227.1#AF159063-1 HAGAX57 1150865 164 blastx.14 (AF176012) J domain gi#5815353<gb>AAD5 100% 192 785 containing protein 1 2650.1#AF176012-1 isoform a [Homo sapiens] HAGAX57 949211 537 HMMER PFAM: DnaJ, prokaryotic PF00226 67.6 224 421 1.8 heat shock protein blastx.14 (AF176012) J domain gi#5815353<gb>AAD5 100% 185 778 containing protein 1 2650.1#AF176012-1 isoform a [Homo sapiens] HANGX15 1177932 165 blastx.14 (AL032657) predicted gi#3881075<emb>CAA 64% 335 565 using Genefinder, similar 21734.1# 52% 560 687 to 1.1 ES 66% 665 736 32% 623 733 45% 674 733 26% 626 751 HANGX15 908849 536 HMMER PFAM: DnaJ domain PF00226 880.1 554 709 2.1 blastx.14 (AL032657) predicted gi#3881075<emb>CAA 51% 506 715 using Genefinder, similar 21734.1# to 1.1 ES HAUBV06 1106041 166 blastx.14 similar to [SwissProt gi#1799806<db>BAA1 98% 1164 2120 Accession Number 6264.1# 80% 2104 2166 P08409] 1 HAUBV06 598802 538 HMMER PFAM: DnaJ C terminal PF01556 262.1 567 932 2.1.1 region HAUBV06 929782 540 HMMER PFAM: DnaJ C terminal PF01556 249.7 16509 1285 2.1.1 region HSBWCM62 908818 541 HMMER PFAM: DnaJ,

prokaryotic PF00226 97.9 37 243 1.8 heat shock protein blastx.14 contains strong similarity gij#1707079#gb#AAB3 42% 19 306 to a DnaJ-like domain 7835.1# (PS:P00536) [Caenorhabditis elegans] HCWFA55 1105672 168 blastx.14 Curved DNA-binding gij#1651491#dbj#BAA3 98% 68 322 protein cbpA [Escherichia 6142.1# colli] HCWFA35 90820 542 HMMER PFAM: DnaJ, prokaryotic PF00226 116.61 80 274 1.8 heat shock protein blastx.14 Curved DNA-binding gij#1651491#dbj#BAA3 98% 68 354 protein cbpA [Escherichia 6142.1# colli] HDACA35 1107236 169 blastx.14 (AK001496) (unnamed gij#7022789#dbj#BAA9 76% 71 904 protein product [Homo 1724.1# sapiens] HDACA35 908837 543 HMMER PFAM: DnaJ, prokaryotic PF00226 65.68 65 229 1.8 heat shock protein blastx.14 cysteine string protein gij#1232185#emb#CAA 49% 80 256 [Bos taurus] 63355.1# HDQGM08 1151469 170 blastx.14 (AF176013) J domain gij#5815355#gb#AAD5 100% 37 357 containing protein 1 2651.1#AF176013-1 isoform b [Homo sapiens] HCQGM08 949210 544 HMMER PFAM: DnaJ, prokaryotic PF00226 68.48 466 269 1.8 heat shock protein blastx.14 (AF176013) J domain gij#5815355#gb#AAD5 100% 505 185 containing protein 1 2651.1#AF176013-1 isoform b [Homo sapiens] HELGB06 1148741 171 blastx.14 ORF-1 [Escherichia coli] gij#402674#gb#AAA18 100% 248 3 299.1# HELGB06 935730 545 HMMER PFAM: DnaJ domain PF00226 78.3 203 421 2.1.1 blastx.14 ORF-1 [Escherichia coli] gij#402674#gb#AAA18 100% 200 445 299.1# HEOPR74 908836 546 HMMER PFAM: DnaJ, prokaryotic PF00226 88.67 65 262 1.8 heat shock protein blastx.14 cysteine string protein gij#1232183#emb#CAA 41% 68 289 [Bos taurus] 63354.1# 50% 457 492 HIBEK35 731480 173 HMMER PFAM: DnaJ domain PF00226 112.7 237 404 2.1.1 HJMAR8 908839 547 HMMER PFAM: DnaJ domain PF00226 42.7 57 149 2.1.1 blastx.14 cysteine string protein 1 - pir#S70515 68% 6 254 human 100% 1 60 HMWGU56 908825 548 HMMER PFAM: DnaJ domain PF00226 126.9 375 569 2.1.1 blastx.14 Similarity to B.subtilis gij#3873707#emb#CAA 59% 327 587 DnaJ protein 1 97416.1# 65% 630 698 [Caenorhabditis elegans] 34% 51 200 HOUDS09 1164010 176 blastx.14 (AK000034) unnamed gij#7019854#dbj#BAA9 66% 2409 659 protein product [Homo 329% 66 375 729 1118 sapiens] 45% 96 167 372 174 248 HOUDS09 949051 549 HMMER PFAM: DnaJ, prokaryotic PF00226 98.53 310 504 1.8 heat shock protein blastx.2 (AK000034) unnamed dbj#BAA90896.1# 53% 37 888 protein product [Homo 55% 899 1033 sapiens] 63% 2 34 HTEKY82 908846 550 HMMER PFAM: DnaJ domain PF00226 119.6 281 475 2.1.1 blastx.14 Similarity to B.subtilis gij#3773707#emb#CAA 53% 236 502 DnaJ protein 1 97416.1# [Caenorhabditis elegans] HTLCY54 1193550 179 blastx.14 MDJ36. sp#Q9QYI74CQYI7 94% 239 460 81% 796 927 81% 484 597 73% 610 699 HTLCY54 908832 551 HMMER PFAM: DnaJ domain PF00226 119.8 245 445 2.1.1 blastx.14 (AB014898) MRJ [Homo] gij#3402485#dbj#BAA3 67% 239 616 sapiens] 2209.1# 78% 797 934 47% 632 694 40% 611 691 HFOXK14 603245 180 HMMER PFAM: Adenylylate and PF0221 137.85 183 401 1.8 Guanylate cyclase catalytic domain HHFFC06 837703 181 HMMER PFAM: Adenylylate and PF00211 386.54 124 708 1.8 Guanylate cyclase catalytic domain HHFLU06 857864 182 HMMER PFAM: Adenylylate and PF00211 108.9 17 268 2.1.1 Guanylate cyclase catalytic domain HAGBA56 732597 183 HMMER PFAM: Eukaryotic protein PF00069 64.9 139 516 2.1.1 kinase domain HAGGF84 911312 184 HMMER PFAM: Eukaryotic protein PF00069 105.85 10 318 1.8 kinase domain blastx.14 ciomadulin-dependent gij#3241849#dbj#BAA2 88% 10 363 protein kinase II-delta 8870.1# 87% 368 413 dash [Oryctolagus 100% 320 364 cuniculus] HAHG033 921782 185 HMMER PFAM: Eukaryotic protein PF00069 83.68 4 564 1.8 kinase domain blastx.14 (AF148590) gij#5052670#gb#AAD3 68% 1 297 BcDNA.LD26657 86% 1#AF145690.1 56% 412 609 [Drosophila melanogaster] \$60% 304 426 36% 676 804 HAHYI08 962113 186 HMMER PFAM: Eukaryotic protein PF00069 74.92 39 278 1.8 kinase domain blastx.14 similar to tyrosine kinase gij#470364#gb#AAC47 44% 192 278 [Caenorhabditis elegans] 047.1# 645 18 92 58% 108 179 HBIOZ10 973131 187 HMMER PFAM: Eukaryotic protein PF00069 121.1 3 365 1.8 kinase domain blastx.2 (AF003134) strong gij#AAB54139.1# 60% 3 305 similarity to the cDC2/COX subfamily of ser/thr protein kinases [Caenorhabditis elegans] HBKD130 729048 188 HMMER PFAM: Eukaryotic protein PF00069 42.23 1 213 1.8 kinase domain HBXW40 706115 189 HMMER PFAM: Eukaryotic protein PF00069 34.01 280 423 1.8 kinase domain HCEHIE35 909837 190 HMMER PFAM: Eukaryotic protein PF00069 30.78 210 347 1.8 kinase domain blastx.14 protein kinase PRK2 gij#914100#gb#AAB33 66% 204 365 [human, DX3 B-cell 346.1# myeloma cell line, Peptide, 964 aa] [Homo sapiens] HCEPW85 911374 191 HMMER PFAM: Eukaryotic protein PF00069 83.52 3 260 1.8 kinase domain blastx.14 predicted using gij#3875903#emb#CAA 87% 3 260 GeneFinder: Similarity to 94127.1# 1 1 1 cDNA HCFAT25 932068 192 HMMER PFAM: Eukaryotic protein PF00069 26.6 136 231 2.1.1 kinase domain blastx.14 (AF096300) HPC/GCK-gij#4322936#gb#AAD1 63% 91 456 like kinase HGK [Homo 6137.1# 72% 60 158 sapiens] 25% 232 212 HCFCF47 1139731 193 blastx.14 (AF003134) strong gij#2088685#gb#AAB5 56% 318 509 similarity to the 4139.1# 71% 736 551 CDC2/CDX1 42% 87 290 61% 15 92 HCFCF47 894415 552 HMMER PFAM: Eukaryotic protein PF00069 89.54 20 295 1.8 kinase domain HDAAV61 81305 194 HMMER PFAM: Eukaryotic protein PF00069 41.11 11 145 1.8 kinase domain HDPKD75 810824 195 HMMER PFAM: Eukaryotic protein PF00069 98.74 68 433 1.8 kinase domain HDPN96 934520 196 HMMER PFAM: Eukaryotic protein PF00069 206.63 3 734 1.8 kinase domain blastx.14 HUMAN NDR gij#2304746#emb#CAA 92% 3 734 [unidentified] 03387.1# HDPSR15 96966 197 HMMER PFAM: Eukaryotic protein PF00069 87.19 351 626 1.8 kinase domain blastx.2 (ABU26288) protein dbj#BAA85045.1# 95% 631 1158 kinase SID6-1512 [Homo 89% 240 692 sapiens] HDQDX20 919027 198 HMMER PFAM: PX domain PF00787 73.4 246 569 2.1.1 blastx.14 serine/threonine protein gij#294637#gb#AAA42 78% 633974 kinase [Rattus norvegicus] 137.1# 44% 455 578 HDQB189 895106 553 HMMER PFAM: Eukaryotic protein PF00069 92.5 260 520 2.1.1 kinase domain HDTBY88 934472

200 HMMER PFAM: Eukaryotic protein PF00069 93.6 3 302 2.1.1 kinase domain blastx.14 p56 KIAMRE protein
 gi|1517820|gb#AAC5 82% 3 170 kinase [Homo sapiens] 0918.1# 35% 192 458 100% 492 509 HE2K207 909948 201
 HMMER PFAM: Eukaryotic protein PF00069 115.19 5 289 1.8 kinase domain blastx.14 (AB004267)
 gi|3135197|dbj#BAAC 96% 17 433 CA[+calmodulin- 8263.1# 56% 418 507 dependent protein kinase I beta 2 [Rattus
 norvegicus] HCBUY74 960914 202 HMMER PFAM: Eukaryotic protein PF00069 36.37 114 407 1.8 kinase domain
 blastx.14 (AF060119) contains gi|3850336|gb#AAC3 36% 117 295 similarity to protein 5524.1# 45% 13 111 kinase 1
 73% 366 410 37% 467 553 HE9N066 974353 203 HMMER PFAM: Eukaryotic protein PF00069 121.6 473 757 1.8 kinase
 domain blastx.14 (AB020741) NIK-related gi|65908519|dbj#BAA8 73% 449 817 kinase [Mus musculus] 4943.1# 94% 2
 263 79% 746 990 HEMBT61 939957 204 HMMER PFAM: Eukaryotic protein PF00069 76.6 16 265 2.1.1 kinase domain
 blastx.2 (AD000992) hypothetical gi|BA051171.1# 71% 13 441 human serine-threonine protein kinase R31240-1 [Homo
 sapiens] HETLF29 909762 205 HMMER PFAM: Eukaryotic protein PF00069 143.18 6 416 1.8 kinase domain blastx.14
 similar to cAMP- gi|3878636|emb#CAA 56% 6 416 dependant protein kinase: 88953.1# cDNA EST 1 1 1 HFUE75
 909758 206 HMMER PFAM: Eukaryotic protein PF00069 85.68 377 664 1.8 kinase domain blastx.14 (AD000092)
 hypothetical gi|1905906|gb#AAB5 43% 362 634 human serine-threonine 1171.1# 46% 632 715 protein kinase R31240-1
 47% 724 774 [Homo sapiens] HFKIT06 934019 207 HMMER PFAM: Eukaryotic protein PF00069 34.65 160 270 1.8
 kinase domain blastx.14 p58 galactosyltransferase- pi|A38282|A38282 51% 178 270 associated protein kinase - 40% 74
 118 human HHEG20 894409 208 HMMER PFAM: Eukaryotic protein PF00069 200.01 26 598 1.8 kinase domain
 HHEHC53 921783 209 HMMER PFAM: Eukaryotic protein PF00069 58.81 507 797 1.8 kinase domain blastx.14
 (AF145690).|gi|5052670|gb#AAD3 79% 567 803 BcDNA.LD28657 8665.1# 33% 397 468 [Arabidopsis thaliana] Ser/Thr
 melanogaster] HHERQ79 944057 210 HMMER PFAM: Eukaryotic protein PF00069 83.4 133 474 1.8 kinase domain
 blastx.2 (AB016589) inducible dbj#BAA85154.1# 90% 109 471 iKappaB kinase [Mus musculus] HISAFA59 959140 211
 HMMER PFAM: Eukaryotic protein PF00069 89.46 3409 771 1.8 kinase domain blastx.14 (AC002343) Ser/Thr
 gi|2262107|gb#AAB6 39% 460 768 protein kinase isolog 3615.1# 33% 397 468 [Arabidopsis thaliana] HKATM10 918665
 212 HMMER PFAM: Eukaryotic protein PF00069 31.4 8 127 2.1.1 kinase domain HLTHP86 919354 213 HMMER PFAM:
 TBC domain PF00566 69.4 855 1274 2.1.1 blastx.2 (AF161420) HSPC302 gb#AAF22890.1#AF1 89% 456 1352 [Homo
 sapiens] 61420-1 99% 1309 1974 55% 1253 1309 HMSJL96 934483 214 HMMER PFAM: Eukaryotic protein PF00069
 26.49 199 363 1.8 kinase domain HMTAJ73 813296 215 HMMER PFAM: Eukaryotic protein PF00069 21.34 4 114 1.8
 kinase domain HNTCP1 9309770 216 HMMER PFAM: Eukaryotic protein PF00069 102.96 445 930 1.8 kinase domain
 blastx.14 (AC006530) unknown gi#4809337#gb#AAD3 55% 463 957 [Homo sapiens] G182.1#AC006530-4 HNTMD79
 934522 217 HMMER PFAM: Eukaryotic protein PF00069 130.82 203 586 1.8 kinase domain blastx.14 LATS [Drosophila
 gi|903942|gb#AAA70 52% 239 586 melanogaster] 336.1# 33% 76 156 57% 169 210 22% 64 240 HNTMH70 757184 218
 HMMER PFAM: Eukaryotic protein PF00069 94.55 176 577 1.8 kinase domain HNTNB14 909942 219 HMMER PFAM:
 Eukaryotic protein PF00069 96.28 36 343 1.8 kinase domain blastx.14 calmodulin-binding gi|349075|gb#AAA16 97% 41
 475 protein [Rattus 633.1# 85% 553 657 norvegicus] 74% 553 657 77% 553 657 69% 559 687 66% 553 667 60% 553
 657 52% 553 654 37% 553 657 39% 553 636 35% 553 645 33% 559 657 77% 512 538 29% 566 557 HODFF88 974911
 220 HMMER PFAM: Eukaryotic protein PF00069 101.43 98 370 1.8 kinase domain blastx.14 mixed-lineage protein
 pi|S32467|JU0229 74% 131 493 kinase 1 - human 81% 763 921 30% 751 915 HOHC47 911586 554 HMMER PFAM:
 HMMER PFAM: Eukaryotic protein PF00069 79.42 211 423 1.8 kinase domain HPCR84 945686 222 HMMER PFAM: Eukaryotic protein
 PF00069 75.57 157 384 1.8 kinase domain blastx.2 similar to protein kinase dbj#BAA11492.1# 78% 127 483 of X.laevis,
 has putative 1 HRACK83 888037 223 HMMER PFAM: Eukaryotic protein PF00069 23.7 4 123 1.8 kinase domain
 HRADM45 717358 224 HMMER PFAM: Eukaryotic protein PF00069 23.7 4 124 1.8 kinase domain blastx.2 (AJ271722)
 putative emb#CAB71 146.1# 98% 2 469 serine/threonine protein kinase MAK-V [Homo sapiens] HRAED74 942527 225
 HMMER PFAM: Eukaryotic protein PF00069 59.6 406 612 1.8 kinase domain blastx.2 (AB023658) dbj#BAA75246.1#
 97% 71 346 Ca/calmodulin-dependent 81% 388 648 protein kinase kinase 71% 342 425 alpha. CaM-kinase kinase 68%
 662 668 alpha [Rattus norvegicus] HHDZ70 942673 226 HMMER PFAM: Eukaryotic protein PF00069 78.2 33 248 2.1.1
 kinase domain blastx.2 kinase like protein emb#CAB10257.1# 39% 33 323 [Arabidopsis thaliana] 50% 303 380 HSKAC24
 823869 227 HMMER PFAM: Eukaryotic protein PF00069 79.36 122 454 1.8 kinase domain HSSMT34 911294 228
 HMMER PFAM: Eukaryotic protein PF00069 53.16 95 292 1.8 kinase domain HT3BG12 921593 229 HMMER PFAM:
 Eukaryotic protein PF00069 27.09 109 183 1.8 kinase domain blastx.14 CYCLIN-DEPENDENT gb#3715668|emb#CAA
 85% 1 246 KINASE (CDK) R 03585.1# [unidentified] HTEGO05 932583 230 HMMER PFAM: Eukaryotic protein PF00069
 50.8 3 232 2.1.1 kinase domain blastx.14 male germ cell-associated gi|205278|gb#AAAAA1 85% 3 395 kinase (mak)
 [Rattus 563.1# 64% 489 761 norvegicus] 55% 768 848 38% 1023 1100 HTEKT33 953308 231 HMMER PFAM: Eukaryotic
 protein PF00069 200.58 428 1393 1.8 kinase domain blastx.2 (AC007661) putative gb#RAD32787.1#AC0 41% 722 1009
 protein kinase 07661-24 36% 1070 1243 [Arabidopsis thaliana] 29% 428 628 HTEMU66 944419 232 HMMER PFAM:
 Eukaryotic protein PF00069 114.85 613 953 1.8 kinase domain blastx.2 MEK Klasse 3 [Mus gb#AAB03535.1# 49% 604
 948 musculus] 29% 209 340 HTEMV09 909843 233 HMMER PFAM: Eukaryotic protein PF00069 93.16 19 312 1.8 kinase
 domain blastx.14 protein kinase I [Rattus gi|406113|gb#AAA19 44% 1 321 norvegicus] 670.1# HTEMV68 1151076 234
 blastx.14 contains EGF-like repeats: gi#495684|gb#AAA50 55% 579 223 highly similar to ZC84.1; 735.1# 44% 783 649 1

diacylglycerol binding domain HDABQ83 669619 572 HMMER PFAM: Phorbol esters / PF00130 6.04 255 284 1.8
 diacylglycerol binding domain HDPDC84 616980 573 HMMER PFAM: Phorbol esters / PF00130 25.6 253 @93 1.8
 diacylglycerol binding domain HDPUF40 121294 265 blastx.14 PTPL1-ASSOCIATED sp|O15463|O15463 54% 286 867
 RHOGAP. 46% 1018 1230 23% 1537 1662 HDPUF40 970586 574 HMMER PFAM: Phorbol esters / PF00130 26.42 415
 546 1.8 diacylglycerol binding domain blastx.14 smitar to C.elegans gi|1504026|dbj|BAA1 94% 61 651 protein [Z37093]
 [Homo 3212.1# 98% 654 806 sapiens] HDPWU07 952734 575 HMMER PFAM: Phorbol esters / PF00130 2.94 333 356
 1.8 diacylglycerol binding domain HDTJJO2 913787 576 HMMER PFAM: Phorbol esters / PF00130 5.7 21 68 1.8
 diacylglycerol binding domain HE2GA18 1121872 268 blastx.14 mhpR [Escherichia coli] gi|1702680|emb|CAA 98% 288
 1 70745.1# HE2GA18 867276 577 HMMER PFAM: Phorbol esters / PF00130 4.09 74 109 1.8 diacylglycerol binding
 domain HE2SY03 947947 578 HMMER PFAM: Phorbol esters / PF00130 2.97 387 437 1.8 diacylglycerol binding domain
 blastx.14 (AF118023) SH3 domain-1 gi4836401#gb#AAD3 46% 456 301 binding protein SNP70 0425.1#AF118023~1
 [Homo sapiens] HELGY64 934511 579 HMMER PFAM: Phorbol esters / PF00130 76.38 241 390 1.8 diacylglycerol
 binding domain HFIIYW31 697730 580 HMMER PFAM: Phorbol esters / PF00130 3.29 29 67 1.8 diacylglycerol binding
 domain HFVIP88 960741 581 HMMER PFAM: Phorbol esters / PF00130 7.32 147 206 1.8 diacylglycerol binding domain
 HGBAS76 771320 582 HMMER PFAM: Phorbol esters / PF00130 3.23 322 348 1.8 diacylglycerol binding domain
 HHEBB62 1151481 274 blastx.14 (AK000193) unnamed gi|7020117|dbj|BAA9 100% 1 375 protein product [Homo
 1000.1# sapiens] HHEBB62 791469 583 HMMER PFAM: Phorbol esters / PF00130 6.2 292 236 1.8 diacylglycerol binding
 domain HHEHU73 923895 584 HMMER PFAM: Phorbol esters / PF00130 4.1 115 156 1.8 diacylglycerol binding domain
 HHEMA11 966924 585 HMMER PFAM: Phorbol esters / PF00130 10.16 354 395 1.8 diacylglycerol binding domain
 HHEQK01 1107392 277 blastx.14 ORF 3 [Homo sapiens] gi|182221|gb#AAA58 37% 165 22 464.1# 55% 266 213 39%
 342 274 HHEQK01 871911 586 HMMER PFAM: Phorbol esters / PF00130 3.27 64 90 1.8 diacylglycerol binding domain
 HHPEM84 915639 278 HMMER PFAM: Phorbol esters / PF00130 12.35 146 187 1.8 diacylglycerol binding domain
 HHSDE64 706739 587 HMMER PFAM: Sterol O- PF01800 276.4 2 364 2.1.1 acyltransferase HIBC94 504326 588
 HMMER PFAM: Phorbol esters / PF00130 3.12 177 206 1.8 diacylglycerol binding domain HKADN55 1220254 281 blastx.
 14 CG5276 PROTEIN. sp|CGVGN8|QVGN 58% 904 1257 8 68% 1465 1617 54% 1279 1437 43% 796 891 63% 754
 810 47% 706 756 87% 1627 1650 42% 102 158 HKADN56 968619 590 HMMER PFAM: Phorbol esters / PF00130 5.32
 207 233 1.8 diacylglycerol binding domain HKXG58 464241 591 HMMER PFAM: Phorbol esters / PF00130 3.59 84 137
 1.8 diacylglycerol binding domain HLCI13 826559 592 HMMER PFAM: Phorbol esters / PF00130 4.83 328 378 1.8
 diacylglycerol binding domain HLTGF17 662405 284 HMMER PFAM: Phorbol esters / PF00130 3.46 136 183 1.8
 diacylglycerol binding domain HLYDC50 1151494 285 blastx.14 similar to C.elegans gi|1504026|dbj|BAA1 59% 275 652
 protein [Z37093] [Homo 3212.1# 52% 719 871 sapiens] 37% 32 127 HLYDC50 677050 593 HMMER PFAM: Phorbol
 esters / PF00130 29.67 191 312 1.8 diacylglycerol binding domain HMADD49 1217031 286 blastx.14 L-aspartate oxidase
 (EC pir#E65035#OXECLD 100% 2212 803 1.4.3.16) nadB [validated] - 1 HMADD49 867481 594 HMMER PFAM: Phorbol
 esters / PF00130 3.79 131 175 1.8 diacylglycerol binding domain HMEKE78 792363 595 HMMER PFAM: Phorbol esters /
 PF00130 3.04 3 35 1.8 diacylglycerol binding domain HMSHU26 681745 596 HMMER PFAM: Phorbol esters / PF00130
 6.77 158 226 1.8 diacylglycerol binding domain HNEEB82 778884 597 HMMER PFAM: Phorbol esters / PF00130 3.33
 126 152 1.8 diacylglycerol binding domain HNIHIA06 859932 598 HMMER PFAM: Phorbol esters / PF00130 3.13 123 146
 1.8 diacylglycerol binding domain HODFY16 95829 599 HMMER PFAM: Phorbol esters / PF00130 3.15 175 213 1.8
 diacylglycerol binding domain HPGQB68 740087 600 HMMER PFAM: Phorbol esters / PF00130 3.9 170 247 1.8
 diacylglycerol binding domain HRDBH04 922022 601 HMMER PFAM: Phorbol esters / PF00130 5.19 600 632 1.8
 diacylglycerol binding domain HSIICF69 531061 602 HMMER PFAM: Phorbol esters / PF00130 3.1 190 213 1.8
 diacylglycerol binding domain HSIQJ94 793624 603 HMMER PFAM: Phorbol esters / PF00130 3.15 207 239 1.8
 diacylglycerol binding domain HSYBL15 1104299 296 blastx.14 (AF021935) myotonic gi|2736151|gb#AAC0 94% 2 931
 dystrophy kinase-related 2941.1# Cdo42-binding kinase [Rattus norvegicus] HSYBL15 660053 604 HMMER PFAM: Phorbol
 esters / PF00130 22.31 2 70 1.8 diacylglycerol binding domain HTEKH29 855660 297 HMMER PFAM: Phorbol
 esters / PF00130 42.4 1660 1803 2.1.1 esters diacylglycerol binding domain (Cl domain) HTGEL46 685425 605 HMMER PFAM: Phorbol
 esters / PF00130 7.26 398 433 1.8 diacylglycerol binding domain HTGFAC5 972982 606 HMMER PFAM: Phorbol
 esters / PF00130 4.17 905 855 1.8 diacylglycerol binding domain blastx.2 phosphatidyl inositol 3-OH kinase (PI3K)
 909 regulatory protein HP-10 - 100% 1080 1259 human 74% 827 1078 100% 67 213 HTLDU61 653016 607 HMMER
 PFAM: Phorbol esters / PF00130 10.67 123 203 1.8 diacylglycerol binding domain HTQF34 527144 608 HMMER PFAM:
 Phorbol esters / PF00130 4.53 233 264 1.8 diacylglycerol binding domain HTTDD46 1152491 302 blastx.14 F10B5.8
 [Caenorhabditis gi|5824432|emb|CAB 74% 32 607 elegans] 54223.1# 70% 623 114 HTTDD46 951114 609 HMMER
 PFAM: Phorbol esters / PF00130 3.36 420 470 1.8 diacylglycerol binding domain blastx.14 F10B5.8 [Caenorhabditis
 gi|5824432|emb|CAB 73% 117 437 elegans] 54223.1# 73% 2 124 HTTIC05 931037 610 HMMER PFAM: Phorbol
 esters / PF00130 4.25 1289 1330 1.8 diacylglycerol binding domain HWHGY45 911621 304 HMMER PFAM: Phorbol
 esters / PF00130 10.67 123 203 1.8 diacylglycerol binding domain HWLQX78 914556 611 HMMER PFAM: Phorbol
 esters / PF00130 4.03 359 391 1.8 diacylglycerol binding domain HWLQX78 914556 611 HMMER PFAM: RhoGAP
 domain PF00620 97.4 715 963 2.1.1 HATDD09 1165331 307 blastx.14 (AK000239) unnamed gi|7020190|dbj|BAA9

52% 3 260 protein product [Homo 1027.1.# sapiens] HATDD09 573794 613 HMMER PFAM: Cyclic nucleotide- PF00027 9.43 59 124 1.6 binding domain HBJGT03 923800 614 HMMER PFAM: Cyclic nucleotide- PF00027 8.96 41 100 binding domain HMTMF45 1141737 309 163.14 [AL109657]J0842G6.1 gi#6691957#emb#CACB 96% 108 377 (novel protein) [Homo 65791.1# 100% 476 700 sapiens] HMTMF45 553382 615 HMMER PFAM: Cyclic nucleotide- PF00027 8.27 230 292 1.8 binding domain HHF0DV86 522953 310 HMMER PFAM: PH domain PF00169 33 196 531 2.1.1 HE8B156 732602 311 HMMER PFAM: Ras family PF0071 46.1 136 246 2.1.1 HJDDH06 907613 318 HMMER PFAM: ADP-ribosylation PF00025 62.3 453 669 2.1.1 factor family blastx.14 [AF143680] arf-like g#449292128gb#AAD3 32% 421 663 protein 2 [Mus musculus] 3908.1[AF143680-1 48% 264 356 HOEJG61 907614 313 HMMER PFAM: ADP-ribosylation PF00025 45.6 399 566 2.1.1 factor family blastx.14 [AF031903] ADP- gi#3687625#gb#AAC6 75% 399 566 ribosylation-like factor 2194.1# 48% 586 652 homolog ARL6 [Mus musculus] HE8PN24 907620 314 HMMER PFAM: ADP-ribosylation PF00025 104.77 197 568 1.8 factors (Arf family) [contains ATP/GTP binding P-loop] blastx.14 ADP-ribosylation factor gi#727191#gb#AAA64 38% 191 430 [Candida albicans] 2661.1# 34% 386 568 HGBH137 907945 315 HMMER PFAM: PH domain PF00169 30.1 107 259 2.1.1 blastx.14 [AF017368] faclogenital gi#3599940#gb#AAC3 82% 14 151 dysplasia protein 2 [Mus 5430.1# 63% 145 201 musculus] HCHOK82 909755 316 HMMER PFAM: RhoGEF domain PF00621 176.8 40 519 2.1.1 blastx.14 [AF017369] faclogenital gi#599942#gb#AAC3 90% 31 849 dysplasia protein 3 [Mus 5431.1# 79% 855 941 musculus] 100% 1062 1082 HFPCH24 912608 317 HMMER PFAM: Ras family PF00071 43.25 47 307 1.8 (contains ATP/GTP binding P-loop) blastx.14 rap2b gene product (AA gi#35863#emb#CAA37 41% 35 229 1-183) [Homo sapiens] 178.1# 40% 337 441 35% 266 325 53% 443 487 HTTKF86 912689 318 HMMER PFAM: Ras family PF00071 29.6 98 223 2.1.1 HCESA79 912709 319 HMMER PFAM: Ras family PF00071 45.1 67 243 2.1.1 blastx.14 [AB027137] RAB-26 gi#5931612#db#ABAA8 92% 52 246 [Homo sapiens] 4707.1# HDTBJ28 912714 320 HMMER PFAM: Ras family PF00071 28.1 137 211.1 blastx.14 Rab12 protein [Cains gi#437985#emb#CAA8 86% 21 98 familiaris] 0471.1# HDPPBF48 912783 321 HMMER PFAM: Ras family PF00071 26.1 33 101 2.1.1 blastx.14 [AL117204] predicted gi#5832782#emb#CAB 48% 123 209 using Genefinder 55120.1# 55% 258 338 [Caenorhabditis elegans] 68% 33 89 53% 429 467 HTPFY65 912928 322 HMMER PFAM: Ras family PF00071 27.2 240 389 2.1.1 blastx.14 similar to the RAS gene gi#1572819#gb#AA80 48% 117 383 family [Caenorhabditis] 9163.1# 60% 398 524 elegans] HMSCM47 923632 323 HMMER PFAM: ATPase PF00004 121.1 65 552 2.1.1 associated with various cellular activities (AAA) blastx.2 [AF038662] Lon protease gbr#AAC05085.16 65% 5 673 [Arabidopsis thaliana] HEOQA56 925132 324 HMMER PFAM: Ras family PF00071 62.8 53 154 1.8 (contains ATP/GTP binding P-loop) blastx.14 GTP-binding protein gi#213115#gb#AAA49 76% 23 202 [Discopyge ornata] 230.1# HTPCQ24 925349 325 HMMER PFAM: PH domain PF00169 31 217 438 2.1.1 HWAIC37 928461 326 HMMER PFA: MCM2/3/5 family PF00493 59.7 8 415 2.1.1 blastx.14 [AL035461]J097N21.5 gi#5334569#emb#CAB 100% 323 415 (novel MCM2/3/5 family 55276.1# 92% 2 85 member) [Homo sapiens] HDFS033 995936 327 HMMER PFAM: A TPases PF0004 47.2 61 399 2.1.1 associated with various cellular activities (AAA) blastx.14 LON1 protease [Zee gi#1816586#gb#AAC5 58% 46 447 may] 0011.1# 62% 855 1200 41% 622 846 36% 580 636 30% 642 710 HLTST63 581528 328 HMMER PFAM: Ras family PF00071 30.6 213 85 2.1.1 HFAAJ44 489201 329 HMMER PFAM: Rhomboid family PF01694 49.5 6 299 2.1.1 HSLMEM4 506804 330 HMMER PFAM: Acrr/AcrD/AcrF PF00873 137.4 2 256 2.1.1 family HETGL79 522826 331 HMMER PFAM: PDZ domain PF00595 281 242 457 2.1.1 (Also known as DHR or GLGF). HFTAR20 670041 332 HMMER PFAM: Glycophan PF01153 17.0 7 12 308 2.1.1 HCUFD32 698379 333 HMMER PFAM: PDZ domain PF00595 29.3 124 369 2.1.1 (Also known as DHR or GLGF). HKAE095 705332 334 HMMER PFAM: PDZ domain PF00595 25.7 239 430 2.1.1 (Also known as DHR or GLGF). HLBWR95 734474 335 HMMER PFAM: PDZ domain PF00595 46.8 270 434 2.1.1 (Also known as DHR or GLGF). HPWCJ63 727553 336 HMMER PFAM: DedA family PF00597 228 235 717 2.1.1 blastx.2 (AE000391) ort, gb#AAC76130.1# 100% 144 803 hypothetical protein [Escherichia coli] HPWCJ63 957495 338 HMMER PFAM: DedA family PF00597 228 1152 670 2.1.1 blastx.2 (AE000391) ort, gb#AAC76130.1# 100% 144 803 hypothetical protein [Escherichia coli] HBXCNN5 782911 337 HMMER PFAM: PDZ domain PF00595 27.5 251 397 2.1.1 (Also known as DHR or GLGF). HJULBN83 857836 338 HMMER PFAM: PDZ domain PF00595 38 133 363 2.1.1 (Also known as DHR or GLGF). HAQET77 885265 339 HMMER PFAM: PF00769 37.6 770 84 2.1.1 Ezrin/radixin/moesin family HMSCZ55 910911 340 HMMER PFAM: PDZ domain PF00595 66.7 276 500 2.1.1 (Also known as DHR or GLGF). blastx.14 [AF090136] lin-7-C gi#3895834#gb#AAC7 89% 3 500 Rattus norvegicus] 8075.1 74% 461 589 HAPOR42 911292 341 HMMER PFAM: PDZ domain PF00595 33.7 456 671 2.1.1 (Also known as DHR or GLGF). blastx.14 [AF061262] semaf gi#3851516#gb#AAC7 98% 249 644 cytoplasmic domain 2310.1# 83% 679 966 associated protein 2 [Mus 80% 968 1012 musculus] 50% 1009 1050 HMTVU910 911449 342 HMMER PFAM: PDZ domain PF00595 66.6 140 394 2.1.1 (Also known as DHR or GLGF). HHTV29 911454 343 HMMER PFAM: PDZ domain PF00595 90.1 180 428 2.1.1 (Also known as DHR or GLGF). blastx.14 [AF034746] LNXp70 gi#3041881#gb#AAC4 55% 150 467 [Mus musculus] 0076.1# 58% 3 146 34% 259 422 80% 552 626 26% 255 413 32% 99 173 HHFJY06 911456 344 HMMER PFAM: PDZ domain PF00595 59.7 99 326 2.1.1 (Also known as DHR or GLGF). blastx.14 [AJ001320] multi PDZ gi#2395979#emb#CAA 40% 132 359 domain protein 1 [Rattus 04881.1# 29% 427 519 norvegicus] HPKIC72 911459 345 HMMER PFAM: PDZ domain PF00595 72 35 260 2.1.1 (Also known as DHR or GLGF). blastx.14 neuroendocrine-dlg gi#1515355#gb#AA86 58% 180 266 [Homo sapiens] 1453.1# 48% 180 260 43% 15 110 40% 105 179 33% 21 110 45% 36 95 40% 114 179 HPIDT84

919878 346 HMMER PFAM: PDZ domain PF00595 225.5 1879 2127 2.1.1 (Also known as DHR or GLGF). blastx.14 (AF034746) LNXp70 gi#30418181rgb#AAC4 88% 256 1455 [Mus musculus] 0076.1# 91% 1774 2151 82% 1462 1782 30% 1462 1728 34% 1597 1779 29% 1876 2121 50% 895 1002 25% 1183 1442 26% 1570 1728 57% 808 849 50% 1504 1545 38% 1507 1596 HMC4V88 924874 347 HMMER PFAM: PDZ domain PF00595 70.4 235 471 2.1.1 (Also known as DHR or GLGF). blastx.14 (AL110228) hypothetical gi#5817167#emb#CAB 41% 232 471 protein [Homo sapiens] 53665.1# 37% 574 645 HKAIP73 928609 348 HMMER PFAM: PDZ domain PF00595 48.9 1041 805 2.1.1 (Also known as DHR or GLGF). blastx.14 (AF131809) Unknown gi#4406542#gb#AAD2 99% 1107 487 [Homo sapiens] 0049.1# HFVHV40 945849 349 HMMER PFAM: Adaptor PF00928 349.2 123 680 2.1.1 complexes medium subunit family blastx.2 clathrin-associated protein gb#AAA37244.1# 98% 108 680 [Mus musculus] HTJN180 952231 350 HMMER PFAM: PDZ domain PF00595 27.1 92 316 2.1.1 (Also known as DHR or GLGF). HEAAE08 959970 351 HMMER PFAM: PDZ domain PF00595 78.5 277 516 2.1.1 (Also known as DHR or GLGF). blastx.14 (AF090133) lin-7-A gi#3885828#gb#AAC7 96% 223 612 [Rattus norvegicus] 8072.1# HDPLU91 963199 352 HMMER PFAM: GNS1/SUR4 PF01151 27.2 452 550 2.1.1 family blastx.2 (AL034374) dJ483K16.1 emb#CAB41293.1# 100% 305 700 (novel protein) [Homo sapiens] HAPRM21 963200 353 HMMER PFAM: GNS1/SUR4 PF01151 43.3 244 378 2.1.1 family blastx.14 (AL034374) dJ483K16.1 gi#4680391#emb#CAB 100% 1 630 (novel protein) [Homo 41293.1# sapiens] HTDAB30 965320 354 HMMER PFAM: Adaptor PF00928 493.4 81 896 2.1.1 complexes medium subunit family H2CBN90 966919 355 HMMER PFAM: PDZ domain PF00595 62.4 609 821 2.1.1 (Also known as DHR or GLGF). blastx.14 (AB005549) atypical PKC gi#3868778#db#BAA3 78% 6 821 specific binding protein 4216.1# [Rattus norvegicus] HETTF47 971305 356 HMMER PFAM: Adaptor PF00928 797.6 75 1325 2.1.1 complexes medium subunit family blastx.14 (AF02797) AP-mu chain gi#4587714#gb#AAD2 99% 60 950 family member mu1B 5870.1# AF020797-1 100% 1155 1328 [Homo sapiens] HADEX52 971351 357 HMMER PFAM: PDZ domain PF00595 63.3 134 388 2.1.1 (Also known as DHR or GLGF). HTADZ74 811489 358 HMMER PFAM: TIR domain PF01582 53.1 305 538 2.1.1 HAPNZ77 887072 359 HMMER PFAM: TIR domain PF01582 31.9 292 483 2.1.1 HELDR74 963001 360 HMMER PFAM: TIR domain PF01582 48.5 492 779 2.1.1 blastx.2 (AF113795) gb#AAF26200.1# AF1 74% 201 1223 toll/interleukin-1 receptor 13795-1 8 [Mus musculus] HDPLJ22 859915 361 HMMER PFAM: Culin family PF00898 391 86 409 2.1.1 HPMLD11 890204 362 HMMER PFAM: Scavenger PF00530 119.6 67 360 2.1.1 receptor cysteine-rich domain HMVDZ78 938574 363 HMMER PFAM: IPT/TIG domain PF01833 52.8 104 244 2.1.1 HTSFJ40 722406 364 HMMER PFAM: GTPase of PF01926 37.5 96 356 2.1.1 unknown function HEMBZ62 742551 365 HMMER PFAM: GTPase of PF01926 42.4 23 176 2.1.1 unknown function HHFGZ38 798591 366 HMMER PFAM: GTPase of PF01928 97.2 338 799 2.1.1 unknown function HDPLN70 854010 367 HMMER PFAM: WH1 domain PF00568 33.1 440 573 2.1.1 HSDJH12 876344 368 HMMER PFAM: GTPase of PF01926 115.7 207 572 2.1.1 unknown function HNBUT01 913838 369 HMMER PFAM: GTPase of PF01926 149.3 30 503 2.1.1 unknown function blastx.14 (AL035532) gi#4481810#emb#CAB 71% 30 506 BACN32G11.d 38482.1# 35% 768 824 [Drosophila melanogaster] HEQON14 923752 370 HMMER PFAM: GTPase of PF01926 33.9 927 562 2.1.1 unknown function blastx.14 (AC002510) unknown gi#2618702#gb#AAB8 54% 951 787 protein [Arabidopsis 4349.1# traliana] HTXKL86 928194 371 HMMER PFAM: GTPase of PF01926 133.3 10 636 2.1.1 unknown function blastx.14 similar to hypothetical gi#2633977#emb#CAB 37% 4 219 proteins [Bacillus subtilis] 13478.1# 33% 493 690 54% 334 405 31% 229 285 30% 355 444 HDQGV77 937546 372 HMMER PFAM: WH1 domain PF00568 140.5 132 458 2.1.1 blastx.14 ana-VASP like protein gi#1644455#gb#AAC5 97% 135 539 [Mus musculus] 2882.1# 78% 711 1157 91% 1215 1358 27% 751 879 35% 1266 1316 26% 1035 1148 33% 890 933 HE8TM80 955022 373 HMMER PFAM: GTPase of PF01926 51.1 460 624 2.1.1 unknown function blastx.14 similar to GTP-binding gi#387819#emb#CAA 59% 463 624 protein; cDNA EST 11 88860.1# 55% 4 90 this gene HWLEY40 957875 374 HMMER PFAM: GTPase of PF01926 103.9 192 632 2.1.1 unknown function blastx.14 (AC002510) unknown gi#2618702#gb#AAB8 54% 1209 1373 protein [Arabidopsis 4349.1# 50% 168 347 thaliana] 70% 516 575 HDPDD36 964320 620 HMMER PFAM: WH1 domain PF00568 32.6 200 361 2.1.1 blastx.14 AE33 protein - fruit fly pir#UC5909#JC5909 46% 170 391 [Drosophila melanogaster] 90% 50 79 HOUBZ94 527876 376 HMMER PFAM: Phosphotyrosine PF00640 41.1 7 129 2.1.1 interaction domain (PTB/PID). HMAIAH32 550977 377 HMMER PFAM: Guanine PF00618 28.9 253 441 2.1.1 nucleotide exchange factor for Ras-like GTPases; N-terminal motif HDPTH43 573418 378 HMMER PFAM: PX domain PF00787 36.5 13 336 2.1.1 HCE3W04 615501 379 HMMER PFAM: RhoGEF domain PF00621 46.1 535 804 2.1.1 HMBUZZ20 670393 380 HMMER PFAM: PX domain PF00787 48.8 2 184 2.1.1 HCPAB51 656665 381 HMMER PFAM: RhoGAP domain PF00620 114.9 402 884 2.1.1 HPJAP28 686349 382 HMMER PFAM: RhoGAP domain PF00620 28.9 302 391 2.1.1 HIBEC79 703000 383 HMMER PFAM: RhoGAP domain PF00620 31.2 308 99 2.1.1 HOQB64 703177 384 HMMER PFAM: Regulator of G Protein 65.6 36.9 48 167 2.1.1 protein signaling domain HTEDL38 761609 385 HMMER PFAM: SAM domain PF00536 56.3 256 441 2.1.1 (Sterile alpha motif) HE9H71 779375 386 HMMER PFAM: SAM domain PF00536 67.7 290 466 2.1.1 (Sterile alpha motif) HNFHS62 779946 387 HMMER PFAM: PX domain PF00787 28.7 53 259 2.1.1 HOJHO89 786548 388 HMMER PFAM: RhoGEF domain PF00621 56 463 750 2.1.1 HFFBB28 844526 389 HMMER PFAM: Domain found in PF00672 43 60 236 2.1.1 bacterial signal proteins HHEWQ81 876083 390 HMMER PFAM: PX domain PF00787 36.5 135 353 2.1.1 HUFHGH9 870778 391 HMMER PFAM: PX domain PF00787 58.6 363 839 2.1.1 HLICA79 880881 392 HMMER PFAM: Domain found in PF00610 79.9 103 327 2.1.1 Dishevelled, Egi-10, and Pleckstrin HSLH01 884251 393 HMMER PFAM: Domain found in

PF00610 30.9 83 304 2.1.1 Dishevelled, Egl-10, and Plectstrin HE9OV91 887364 394 HMMEF PFAM: SPRY domain PF00622 80.6 313 633 2.1.1 HHEDS585 994602 395 HMMEF PFAM: RhoGAP domain PF00620 28.2 11 121 2.1.1 HNTDJ66 899624 396 HMMEF PFAM: SAM domain PF00536 42.3 1375 1569 2.1.1 (Sterile alpha motif) HKAHO77 906671 397 HMMEF PFAM: RhoGAP domain PF00620 24.7 63 248 2.1.1 blastx.14 GTPASE-ACTIVATING gln276305#emb#CAB 69% 54 171 PROTEIN [Homo 06085.1# 95% 180 248 sapiens] 95% 248 319 100% 417 47 72% 313 366 81% 497 544 81% 4 36 81% 481 513 HTFNP84 909687 398 HMMEF PFAM: RhoGEF domain PF00621 84.7 70 405 2.1.1 blastx.14 ec12 [Mus musculus] gln293332#gb#AAA37 91% 73 1131 536.1# 62% 1042 1227 100% 27 56 17% 62 265 HDQZG78 909735 399 HMMEF PFAM: RhoGEF domain PF00621 85.2 5 277 2.1.1 blastx.14 (AF038388) actin-gln3342246#gb#AAC2 93% 5 442 filament binding protein 7698.1# Frabin [Rattus norvegicus] HHEDM52 909742 400 HMMEF PFAM: RhoGEF domain PF00621 64.3 1295 1501 2.1.1 blastx.14 (AF017369) faclogonital gln359942#gb#AAC3 70% 998 1510 dysplasia protein 3 [Mus 5431.1# 62% 854 982 musculus] 100% 1516 1545 80% 815 844 77% 1573 1598 HSDQ38 909854 401 HMMEF PFAM: RhoGAP domain PF00620 175.6 270 686 2.1.1 blastx.14 carboxyl terminus of the gln3874826#emb#CAA 37% 381 659 predicted protein shows 1 86318.1# 55% 270 350 1 comes from this gene: 25% 654 737 cDNA EST 33% 14 67 EMBL:D32994 comes from this gene HSKBF02 909855 402 HMMEF PFAM: RhoGAP domain PF00620 130.6 9 386 2.1.1 blastx.14 p115 [Homo sapiens] gln840786#emb#CAA5 59% 6 386 5394.1# 66% 364 390 HIBDE74 90987 621 HMMEF PFAM: RhoGEF domain PF00621 152.7 44 604 2.1.1 blastx.14 (AB001770) PEM-2 gln4107011#dbj#BAA3 58% 429 628 [Ciona savignyi] 6290.1# 41% 161421 33% 29 127 HWMAE53 909877 404 HMMEF PFAM: RhoGEF domain PF00621 53 112 267 2.1.1 blastx.14 (AF132481) Eset1. gln4378891#gb#AAD1 44% 112 285 protein [Mus musculus] 9749.1# HFXCQ26 909961 405 HMMEF PFAM: RasGEF domain PF00617 162.7 225 593 2.1.1 blastx.14 (AL080117) hypothetical gln5262547#emb#CAB 93% 225 593 protein [Homo sapiens] 45716.1# 50% 149 220 HFTCU45 910058 406 HMMEF PFAM: RhoGEF domain PF00621 80.9 82 474 2.1.1 blastx.14 Trio [Homo sapiens] gln3552970#gb#AAC3 70% 1 501 4245.1# 41% 34 387 35% 421 540 57% 466 529 HFTBL33 91055 407 HMMEF PFAM: RhoGEF domain PF00621 40.3 223 387 2.1.1 blastx.14 (AF091395) Trio isoform gln3644048#gb#AAC4 60% 199 483 [Homo sapiens] 3042.1# 61% 31 207 55% 703 840 67% 586 687 33% 596 786 42% 334 483 31% 37 189 47% 199 267 35% 1128 1187 46% 1175 1219 HTXJA84 911387 408 HMMEF PFAM: Fes/CIP4 PF00611 42.2 101 373 2.1.1 homology domain blastx.14 macrophage actin-gln3947712#emb#CAA 68% 80 604 associated-tyrosine- 77027.1# 82% 592 726 phosphorylated protein 60% 725 808 [Mus musculus] HKAAW89 911389 409 HMMEF PFAM: Fes/CIP4 PF00611 44.7 88 345 2.1.1 homology domain HSXDD55 911460 410 HMMEF PFAM: RasGEF domain PF00617 146.2 933 695 2.1.1 blastx.14 similar to phorbol ester gln3876235#emb#CAA 38% 285 808 and DAG binding domain; 94755.1# 66% 657 904 1 HUFIC14 911558 411 HMMEF PFAM: RhoGAP domain PF00620 158 3 500 2.1.1 blastx.14 similar to C.elegans gln1504026#dbj#BAA1 87% 3 773 protein [Z37093] [Homo 3212.1# 50% 8 43 sapiens] HWAFT4 911559 412 HMMEF PFAM: RhoGAP domain, PF00620 34.3 34 135 2.1.1 blastx.14 similar to C.elegans gln1504026#dbj#BAA1 90% 40 702 protein [Z37093] [Homo 3212.1# sapiens] HETCL18 914535 413 HMMEF PFAM: Domain found in PF00610 79.9 19 240 2.1.1 Dishevelled, Egl-10, and Plectstrin blastx.2 (AF115480) cAMP-gln#AAD09132.1# 39% 28 276 dependent Rap1 guanine- nucleotide exchange factor [Mus musculus] HCRNK75 914536 414 HMMEF PFAM: Domain found in PF00610 79.9 2006 1782 2.1.1 Dishevelled, Egl-10, and Plectstrin blastx.2 (AF115480) cAMP- gb#AAD09132.1# 36% 226 525 dependent Rap1 guanine- 35% 1077 1790 nucleotide exchange] factor [Mus musculus] HTPFA03 922785 415 HMMEF PFAM: RhoGAP domain PF00620 54.5 2 292 2.1.1 blastx.14 (AC004794) F02569-2 gln3184264#gb#AAC1 84% 50 295 [Homo sapiens] 8917.1# HWARD60 926487 416 HMMEF PFAM: RhoGAP domain PF00620 148.8 51 605 2.1.1 blastx.14 (AF003389) contains gln208864#gb#AAC7 33% 297 611 similarity to N-chimaerins 1136.1# 30% 33 275 [Caenorhabditis elegans] HWLFJ01 928017 417 HMMEF PFAM: Phosphotyrosine PF00640 40.6 202 612 2.1.1 interaction domain (PTB/PID). blastx.14 (AL117654) hypothetical gln5912247#emb#CAB 91% 43 675 protein protein [Mus musculus] 56030.1# 46% 691 774 37% 683 763 HTXNG95 928577 418 HMMEF PFAM: SPRY domain PF00622 105.7 208 585 2.1.1 blastx.14 zine finger protein [Mus gln406748#emb#CAA5 57% 139 492 musculus] 3092.1# 54% 52 123 81% 541 579 HPCIG66 930886 419 HMMEF PFAM: SPRY domain PF00622 80.4 90 455 2.1.1 blastx.14 (AC007019) hypothetical gln417294#gb#AAD2 46% 57 377 protein [Arabidopsis 0419.1# 51% 378 464 thaliana] 50% 825 866 38% 550 603 52% 780 830 HCRPUJ7 931140 420 HMMEF PFAM: RhoGAP domain PF00620 94.9 514 715 2.1.1 blastx.2 similar to human GTPase gln#BAA13442.1# 97% 77 799 activating protein(A49895) [Homo sapiens] HEGRT95 934556 421 HMMEF PFAM: RhoGAP domain PF00620 36.8 1 231 2.1.1 blastx.14 carboxyl terminus of the gln3874826#emb#CAA 34% 1 237 predicted protein shows 1 86318.1# 1 comes from this gene: cDNA EST EMBL:D32994 comes from this gene HFXJM13 935725 422 HMMEF PFAM: PX domain PF00787 35.8 85 393 2.1.1 blastx.14 similar to RNA gln3879784#emb#CAA 41% 184 343 recognition motif. (aka 93419.1# 40% 66 155 RRM, RBD, or 11 HDPWU37 940705 423 HMMEF PFAM: RhoGAP domain PF00620 50.2 2 116 2.1.1 blastx.14 similar to SH3-binding gln4826478#emb#CAB 79% 3 491 protein [Homo sapiens] 42696.1# 77% 503 529 66% 509 535 HHSDL85 942248 424 HMMEF PFAM: RasGEF domain PF00617 31 2 55 2.1.1 blast.2 (AF053308) putative gb AAC06257.1 50% 2 472 guanine nucleotide releasing factor [Drosophila affinis] HTJMD31 942848 425 HMMEF PFAM: SPRY domain PF00622 40.2 58 423 2.1.1 blastx.14 (AL117386) putative gln588179 emb CAB 33% 49 279 protein [Arabidopsis 55697.1 thaliana] HWADD57 943039 426 HMMEF PFAM: GTPase-activator PF00616 56.1 2 12

343 2.1.1 protein for Ras-like GTPase blastx.14 (AB016962) synGAP-b1 gi 4417207 dbj BAA7 45% 116 598 [Rattus norvegicus] 4972.1 69% 2 70 35% 739 855 HLWAH05 944904 427 HMMER PFAM: RhoGAP domain PF00620 224.3 470 924 2.1.1 blastx 2 dJ37E18.2(SH3-domain emb CAB42896.1 96% 413 1291 binding protein 1) [Homo sapiens] 66 428 sapiens] 41% 1103 1245 31% 1091 1258 26% 1091 1327 30% 1100 1273 37% 1103 1228 28% 733 924 26% 1040 1058 30% 721 834 20% 1046 1267 26% 999 1136 HDPC184 945527 428 HMMER PFAM: RhoGAP domain PF00620 103.4 85 519 2.1.1 blastx.2 (AK001174) unnamed dbj BAA91533.1 43% 64 882 protein product [Homo sapiens] HBXDJ07 946830 429 HMMER PFAM: Synaptophysin/PF01284 406.7 125 604 2.1.1 synaptophysin blastx.2 synaptophysin - rat pil JH0300 JH0300 90% 125 643 91% 610 921 HAMFD12 952436 430 HMMER PFAM: Guanine PF00618 40.7 3 77 2.1.1 nucleotide exchange factor for Ras-like GTPases; N-terminal motif blastx. 14 guanine nucleotide gi 193673 gb AAA37 84% 3 434 dissociation stimulator 714.1 [Mus musculus] HFKHR40 952470 431 HMMER PFAM: RhoGAP domain PF00620 88.9 1376 1708 2.1.1 blastx. 14 carboxyl terminus of the gi 3874826 emb CAA 46% 1319 1498 predicted protein shows 1 86318.1 49% 1683 1865 1 comes from this gene ; 81% 1583 1630 cDNA EST 47% 232 300 EMBL:D32994 comes 37% 1253 1324 from this gen 23% 962 1078 37% 1211 1282 50 % 643 696 HDTA108 953265 432 HMMER PFAM: SAM domain PF00536 29.1 367 534 2.1.1 (Sterile alpha motif) HMKCX80 956254 433 HMMER PFAM: PX domain PF00787 47.3 425 613 2.1.1 blastx. 14 Unknown gene product gi 3417291 gb AAC3 96% 613 699 [Homo sapiens] 1664.1 68% 533 607 HCEMF69 961308 434 HMMER PFAM: PX domain PF00787 54.8 14 247 2.1.1 HWLHF10 963422 435 HMMER PFAM: RhoGAP domain PF00520 121 640 975 2.1.1 blastx.14 similar to SH3-binding gi 4826478 emb CAB 49% 661 978 protein [Homo sapiens] 42896.1 435 349 591 38% 118 339 68% 592 696 30% 536 604 HOEMG82 963855 436 HMMER PFAM: IQ calmodulin- PF00612 64.9 230 292 2.1.1 binding motif HFXDR37 965915 437 HMMER PFAM: PX domain PF00787 39.9 1437 1189 2.1.1 blastx. 14 (AF121862) sorting nexin gi 4689264 gb AAD2 35% 957 631 13 [Homo sapiens] 7635.1 AF121862-1 36% 1002 928 33% 2263 2174 HNNAS46 969470 438 HMMER PFAM: Ras-like GTPase blastx. 14 232 673 2.1.1 blastx. 14 (AF121858) sorting nexin gi 4689256 gb AAD2 99% 770 1435 8 [Homo sapiens] 7831.1 AF121858 1 99% 136 768 HRAAS26 971219 439 HMMER PFAM: PX domain PF00787 52.9 89 367 2.1.1 blastx.14 (AF 139461) hypothetical gi 4894946 gb AAD3 100% 59 499 protein SBB131 [Homo 2668.1 AF 139461-1 sapiens] HIHEL28 973096 440 HMMER PFAM: GTPase-activator PF00616 47.4 148 372 2.1.1 protein for Ras-like GTPase blastx. 14 (AF047711) nGAP gi 4105589 gb AAD0 51% 4 375 [Homo sapiens] 4814.1 HCETF22 973334 441 HMMER PFAM: Diacylglycerol PF00781 202.1 112 468 2.1.1 kinase catalytic domain (presumed) HCMSF55 975260 623 HMMER PFAM: PDZ domain PF00595 69.3 154 393 2.1. (Also known as DHR or GLGF).

[60] Table 2 further characterizes certain encoded polypeptides of the invention, by providing the results of comparisons to protein and protein family databases. The first column provides a unique clone identifier, "Clone ID NO.", corresponding to a cDNA clone disclosed in Table 1A. The second column provides the unique contig identifier, "Contig ID.", which allows correlation with the information in Table 1A. The third column provides the sequence identifier, "SEQ ID NO.", for the contig polynucleotide sequences. The fourth column provides the analysis method by which the homology/identity disclosed in the Table was determined. The fifth column provides a description of the PFAM/NR hit identified by each analysis. Column six provides the accession number of the PFAM/NR hit disclosed in the fifth column. Column seven, score/percent identity, provides a quality score or the percent identity, of the hit disclosed in column five. Comparisons were made between polypeptides encoded by polynucleotides of the invention and a non-redundant protein database (herein referred to as "NR"), or a database of protein families (herein referred to as "PFAM"), as described below.

[61] The NR database, which comprises the NBRF PIR database, the NCBI GenPept database, and the SIB SwissProt and TrEMBL databases, was made non-redundant using the computer program nrdb2 (Warren Gish, Washington University in Saint Louis). Each of the polynucleotides shown in Table 1A, column 3 (e.g., SEQ ID NO: X or the Query sequence) was used to search against the NR database. The computer program BLASTX was used to compare a 6-frame translation of the Query sequence to the NR database (for information about the BLASTX algorithm please see Altschul et al., J. Mol. Biol. 215 : 403-410 (1990) ; and Gish and States, Nat. Genet. 3 : 266-272 (1993). A description of the sequence that is most similar to the Query sequence (the highest scoring 'Subject') is shown in column five of Table 2 and the database accession number for that sequence is provided in column six. The highest scoring 'Subject' reported in Table 2 if (a) the estimated probability that the match occurred by chance alone is less than 1. 0e-07, and (b) the match was not to a known repetitive element. BLASTX returns alignments of short polypeptide segments of the Query and Subject sequences which share a high degree of similarity ; these segments are known as High-Scoring Segment Pairs or HSPs. Table 2 reports the degree of similarity between the Query and the Subject for each HSP as a percent identity in Column 7. The percent identity is determined by dividing the number of exact matches between the two aligned sequences in the HSP, dividing by the number of Query amino acids in the HSP and multiplying by 100.

The polynucleotides of SEQ ID NO: X which encode the polypeptide sequence that generates an HSP are delineated by columns 8 and 9 of Table 2.

[62] The PFAM database, PFAM version 2.1, (Sonnhammer et al., Nucl. Acids Res., 26 : 320-322, 1998) consists of a series of multiple sequence alignments; one alignment for each protein family. Each multiple sequence alignment is converted into a probability model called a Hidden Markov Model, or HMM, that represents the position-specific variation among the sequences that make up the multiple sequence alignment (see, e.g., Durbin et al.,

 Biological sequence analysis : probabilistic models of proteins and nucleic acids, Cambridge University Press, 1998 for the theory of HMMs). The program HMMER version 1.8 (Sean Eddy, Washington University in Saint Louis) was used to compare the predicted protein sequence for each Query sequence (SEQ ID NO : Y in Table 1A) to each of the HMMs derived from PFAM version 2.1. A HMM derived from PFAM version 2.1 was said to be a significant match to a polypeptide of the invention if the score returned by HMMER 1.8 was greater than 0.8 times the HMMER 1.8 score obtained with the most distantly related known member of that protein family. The description of the PFAM family which shares a significant match with a polypeptide of the invention is listed in column 5 of Table 2, and the database accession number of the PFAM hit is provided in column 6. Column 7 provides the score returned by HMMER version 1.8 for the alignment. Columns 8 and 9 delineate the polynucleotides of SEQ ID NO : X which encode the polypeptide sequence which show a significant match to a PFAM protein family.

[63] As mentioned, columns 8 and 9 in Table 2, "NT From" and "NT To", delineate the polynucleotides of SEQ ID NO : X that encode a polypeptide having a significant match to the PFAM/NR database as disclosed in the fifth column. In one embodiment, the invention provides a protein comprising, or alternatively consisting of, a polypeptide encoded by the polynucleotides of SEQ ID NO : X delineated in columns 8 and 9 of Table 2. Also provided are polynucleotides encoding such proteins, and the complementary strand thereto.

[64] The nucleotide sequence SEQ ID NO : X and the translated SEQ ID NO : Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, the nucleotide sequences of SEQ ID NO : X are useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO : X or the cDNA contained in Clone ID NO : Z. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling immediate applications in chromosome mapping, linkage analysis, tissue identification and/or typing, and a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO : Y may be used to generate antibodies which bind specifically to these polypeptides, or fragments thereof, and/or to the polypeptides encoded by the cDNA clones identified in, for example, Table 1A.

[65] Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

[66] Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO : X, and a predicted translated amino acid sequence identified as SEQ ID NO : Y, but also a sample of plasmid DNA containing cDNA Clone ID NO : Z (deposited with the ATCC on October 5, 2000, and receiving ATCC designation numbers PTA 2574 and PTA 2575 ; deposited with the ATCC on January 5, 2001, and having depositor reference numbers TS-1, TS-2, AC-1, and AC-2 ; and/or as set forth, for example, in Table 1A, 6 and 7). The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. Further, techniques known in the art can be used to verify the nucleotide sequences of SEQ ID NO : X.

[67] The predicted amino acid sequence can then be verified from such deposits.

Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

RACE Protocol For Recovery of Full-Length Genes [68] Partial cDNA clones can be made full-length by utilizing the rapid amplification of cDNA ends (RACE) procedure described in Frohman, M. A., et al., Proc. Nat'l. Acad. Sci.

USA, 85-8998-9002 (1988). A cDNA clone missing either the 5' or 3' end can be reconstructed to include the absent base pairs extending to the translational start or stop codon, respectively. In some cases, cDNAs are missing the start codon of translation, therefore. The following briefly describes a modification of this original 5'RACE procedure.

Poly A+ or total RNA is reverse transcribed with Superscript II (Gibco/BRL) and an antisense or complementary primer specific to the cDNA sequence. The primer is removed from the reaction with a Microcon Concentrator (Amicon). The first-strand cDNA is then tailed with dATP and terminal deoxynucleotidyl transferase (Gibco/BRL). Thus, an anchor sequence is produced which is needed for PCR amplification. The second strand is synthesized from the dA-tail in PCR buffer, Taq DNA polymerase (Perkin-Elmer Cetus), an oligo-dT primer containing three adjacent restriction sites (XhoI, Sali and ClaI) at the 5' end and a primer containing just these restriction sites. This double-stranded cDNA is PCR amplified for 40 cycles with the same primers as well as a nested cDNA-specific antisense primer. The PCR products are size-separated on an ethidium bromide-agarose gel and the region of gel containing cDNA products the predicted size of missing protein-coding DNA is removed. cDNA is purified from the agarose with the Magic PCR Prep kit (Promega), restriction digested with XhoI or Sali, and ligated to a plasmid such as pBlueScript SKII (Stratagene) at XhoI and EcoRV sites. This DNA is transformed into bacteria and the plasmid clones sequenced to identify the correct protein-coding inserts. Correct 5' ends are confirmed by comparing this sequence with the putatively identified homologue and overlap with the partial cDNA clone. Similar methods known in the art and/or commercial kits are used to amplify and recover 3' ends.

[69] Several quality-controlled kits are commercially available for purchase. Similar reagents and methods to those above are supplied in kit form from Gibco/BRL for both 5' and 3' RACE for recovery of full length genes. A second kit is available from Clontech which is a modification of a related technique, SLIC (single-stranded ligation to single-stranded cDNA), developed by Dumas et al., *Nucleic Acids Res.*, 19 : 5227-32 (1991). The major differences in procedure are that the RNA is alkaline hydrolyzed after reverse transcription and RNA ligase is used to join a restriction site-containing anchor primer to the first-strand cDNA. This obviates the necessity for the dA-tailing reaction which results in a polyT stretch that is difficult to sequence past.

[70] An alternative to generating 5' or 3' cDNA from RNA is to use cDNA library double-stranded DNA. An asymmetric PCR-amplified antisense cDNA strand is synthesized with an antisense cDNA-specific primer and a plasmid-anchored primer. These primers are removed and a symmetric PCR reaction is performed with a nested cDNA-specific antisense primer and the plasmid-anchored primer.

RNA Ligase Protocol For Generating The 5' or 3' End Sequences To Obtain Full Length Genes [71] Once a gene of interest is identified, several methods are available for the identification of the 5' or 3' portions of the gene which may not be present in the original cDNA plasmid. These methods include, but are not limited to, filter probing, clone enrichment using specific probes and protocols similar and identical to 5' and 3' RACE.

While the full length gene may be present in the library and can be identified by probing, a useful method for generating the 5' or 3' end is to use the existing sequence information from the original cDNA to generate the missing information. A method similar to 5' RACE is available for generating the missing 5' end of a desired full-length gene. (This method was published by Fromont-Rachine et al., *Nucleic Acids Res.*, 21 (7) : 1683-1684 (1993)). Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcript and a primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest, is used to PCR amplify the 5' portion of the desired full length gene which may then be sequenced and used to generate the full length gene. This method starts with total RNA isolated from the desired source, poly A RNA may be used but is not a prerequisite for this procedure. The RNA preparation may then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase if used is then inactivated and the RNA is treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation can then be used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction can then be used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the relevant gene.

[72] The present invention also relates to vectors or plasmids which include such DNA sequences, as well as the use of the DNA sequences. The material deposited with the ATCC (deposited with the ATCC on October 5, 2000, and receiving ATCC designation numbers PTA 2574 and PTA 2575; deposited with the ATCC on January 5, 2001, and receiving ATCC designation numbers TS-1, TS-2, AC-1, and AC-2; and/or as set forth, for example, in Table 1A, Table 6, or Table 7) is a mixture of cDNA clones derived from a variety of human tissue and cloned in either a plasmid vector or a phage vector, as described, for example, in Table 7. These deposits are referred to as "the deposits" herein. The tissues from which some of the clones were derived are listed in Table 7, and the vector in which the corresponding cDNA is contained is also indicated in Table 7. The deposited material includes cDNA clones corresponding to SEQ ID NO : X described, for example, in Table 1A (Clone ID NO : Z). A clone which is isolatable from the ATCC Deposits by use of a sequence listed as SEQ ID NO : X, may include the entire coding region of a human gene or in other cases such clone may include a substantial portion of the coding region of a human gene.

Furthermore, although the sequence listing may in some instances list only a portion of the DNA sequence in a clone included in the ATCC Deposits, it is well within the ability of one skilled in the art to sequence the DNA included in a clone contained in the ATCC Deposits by use of a sequence (or portion thereof) described in, for example Tables 1A or 2 by procedures hereinafter further described, and others apparent to those skilled in the art.

[73] Also provided in Table 7 is the name of the vector which contains the cDNA clone. Each vector is routinely used in the art. The following additional information is provided for convenience.

[74] Vectors Lambda Zap (U. S. Patent Nos. 5, 128, 256 and 5, 286, 636), Uni-Zap XR (U. S. Patent Nos. 5, 128, 256 and 5, 286, 636), Zap Express (U. S. Patent Nos. 5, 128, 256 and 5, 286, 636), pBluescript (pBS) (Short, J. M. et al., *Nucleic Acids Res.* 16 : 7583-7600 (1988); Altling-Mees, M. A. and Short, J. M., *Nucleic Acids Res.* 17 : 9484 (1989)) and pBK (Altling-Mees, M. A. et al., *Strategies* 5 : 58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into E. coli strain XL-1 Blue, also available from Stratagene.

[75] Vectors pSport1, pCMVSport 2.0 and pCMVSport 3.0, were obtained from Life Technologies, Inc., P. O. Box 5009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., *Focus* 15 : 59- (1993). Vector lacMid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue.

Vector pCR&comat2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., *Nuc. Acids Res.*

16 : 9577-9586 (1988) and Mead, D. et al., *Bio/Technology* 9 : (1991).

[76] The present invention also relates to the genes corresponding to SEQ ID NO : X, SEQ ID NO : Y, and/or the deposited clone (Clone ID NO : Z). The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein.

Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

[77] Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO : X or the complement thereof, polypeptides encoded by genes corresponding to SEQ ID NO : X or the complement thereof, and/or the cDNA contained in Clone ID NO : Z, using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences

provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

[76] The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

[79] The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

[80] The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one- step method described in Smith and Johnson, Gene 67 : 31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the polypeptides of the present invention in methods which are well known in the art.

[81] The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO : X, and/or the cDNA sequence contained in Clone ID NO : Z. The present invention also provides a polypeptide comprising, or alternatively consisting of, the polypeptide sequence of SEQ ID NO : Y, a polypeptide encoded by SEQ ID NO : X or a complement thereof, a polypeptide encoded by the cDNA contained in Clone ID NO : Z, and/or the polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO : B as defined in column 6 of Table 1B. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of the polypeptide sequence of SEQ ID NO : Y, a polypeptide encoded by SEQ ID NO : X, a polypeptide encoded by the cDNA contained in Clone ID NO : Z, and/or a polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO : B as defined in column 6 of Table 1B are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of, the complement of the nucleic acid sequence of SEQ ID NO : X, a nucleic acid sequence encoding a polypeptide encoded by the complement of the nucleic acid sequence of SEQ ID NO : X, and/or the cDNA contained in Clone ID NO : Z.

[82] Moreover, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in Table 1B column 6, or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand (s) of the sequences delineated in Table 1B column 6, or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO : B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO : A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO : A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above- described polynucleotides and polypeptides are also encompassed by the invention.

[83] Further, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO : Z (see Table 1B, column 1), or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand (s) of the sequences delineated in column 6 of Table 1B which

correspond to the same Clone ID NO : Z (see Table 1B, column 1), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO : Z (see Table 1B, column 1) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO : B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO : Z (see Table 1B, column 1) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO : A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO : Z (see Table 1B, column 1) and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO : A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

[84] Further, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO : X (see Table 1B, column 2), or any combination thereof. Additional representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand (s) of the sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO : X (see Table 1B, column 2), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO : X (see Table 1B, column 2) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO : B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO : X (see Table 1B, column 2) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO : A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO : X (see Table 1B, column 2) and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO : A (see Table 1B, column 4).

Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

[85] Moreover, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of Table 1B column 6, or any combination thereof.

Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand (s) of the sequences delineated in the same row of Table 1B column 6, or any combination thereof. In preferred embodiments, the polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand (s) of the sequences delineated in the same row of Table 1B column 6, wherein sequentially delineated sequences in the table (i. e. corresponding to those exons located closest to each other) are directly contiguous in a 5' to 3' orientation. In further embodiments, above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1B, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO : B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1B, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO : A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1B, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO : A (see Table 1B, column 4).

Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[86] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B, and the polynucleotide sequence of SEQ ID NO : X (e. g., as defined in Table 1B, column 2) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[87] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO : Z (see Table 1B, column 1), and the polynucleotide sequence of SEQ ID NO : X (e. g., as defined in Table 1A or 1B) or fragments or variants thereof. In preferred embodiments, the delineated sequence (s) and polynucleotide sequence of SEQ ID NO : X correspond to the same Clone ID NO : Z. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[88] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of column 6 of Table 1B, and the polynucleotide sequence of SEQ ID NO : X (e. g., as defined in Table 1A or 1B) or fragments or variants thereof. In preferred embodiments, the delineated sequence (s) and polynucleotide sequence of SEQ ID NO : X correspond to the same row of column 6 of Table 1B. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[89] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3'10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5'10 polynucleotides of the sequence of SEQ ID NO : X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention.

Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[90] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3'10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5'10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO : X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[91] In specific embodiments, polynucleotides of the invention or alternatively consist of, a polynucleotide sequence in which the 3'10 polynucleotides of the sequence of SEQ ID NO : X and the 5'10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1B are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[92] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide

sequence in which the 3'10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO : X and the 5'10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1B are directly contiguous.

Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides, are also encompassed by the invention.

[93] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3'10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5'10 polynucleotides of another sequence in column 6 are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention.

Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[94] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3'10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5'10 polynucleotides of another sequence in column 6 corresponding to the same Clone ID NO : Z (see Table 1B, column 1) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[95] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3'10 polynucleotides of one sequence in column 6 corresponding to the same contig sequence identifier SEQ ID NO : X (see Table 1B, column 2) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention.

Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[96] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3'10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5'10 polynucleotides of another sequence in column 6 corresponding to the same row are directly contiguous. In preferred embodiments, the 3'10 polynucleotides of one of the sequences delineated in column 6 of Table 1B is directly contiguous with the 5'10 polynucleotides of the next sequential exon delineated in Table 1B, column 6. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[97] Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence

databases and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. Accordingly, for each contig sequence (SEQ ID NO : X) listed in the fourth column of Table 1A, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 and the final nucleotide minus 15 of SEQ ID NO : X, b is an integer of 15 to the final nucleotide of SEQ ID NO : X, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO : X, and where b is greater than or equal to a + 14. More specifically, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a and b are integers as defined in columns 4 and 5, respectively, of Table 3. In specific embodiments, the polynucleotides of the invention do not consist of at least one, two, three, four, five, ten, or more of the specific polynucleotide sequences referenced by the Genbank Accession No. as disclosed in column 6 of Table 3 (including for example, published sequences in connection with a particular BAC clone), in further embodiments, preferably excluded from the invention are the specific polynucleotide sequence (s) contained in the clones corresponding to at least one, two, three, four, five, ten, or more of the available material having the accession numbers identified in the sixth column of this Table (including for example, the actual sequence contained in an identified BAC clone). In no way is this listing meant to encompass all of the sequences which may be excluded by the general formula, it is just a representative example. All references available through these accessions are hereby incorporated by reference in their entirety.

TABLE 3 SEQ EST Disclaimer Clone ID NO: Contig Range of a Range of b NO:Z X ID: Accession #'s HDPTE21 11 1165661-1-4732 15-4746 HEDR51 12 1197894-1-2300 15-2314 L HAPRA41 13 1154054-1-1264 15-1278 HEBX017 14 1171958-1-339 15-353 HBCX38 15 910086-1-2160 15-2174 A1752485, A1804792, A1439106, A1971133, A1991958, A1752484, A1432296, A1756420, A9028219, A1912373, R69026, A894797, A1554161, A1752414, A113307, A1248165, R61527, N62403, R69727, N47856, A1689339, A1365569, R61583, A1984780, AA219502, H44175, A1802627, A1752415, T32963, AW295386, AA985168, H06745, A40750, M79099, AA203312, R00511, A91842, A91846, A91844, and A91846. HCE350 16 1227586-1-3775 15-3789 HCEQD04 17 1150868-1-625 15-639 HDPH92 18 909090-1-2933 15-2947 AC056341, HDPLT89 19 962403-1-2437 15-2451 HDPUSU48 20 1228264-1-2802 15-2916 HDPVWE80 21 909916-1-932 15-946 HDQFY84 22 1092137-1-3253 15-3267 HEONO19 23 930705-1-897 15-911 HFCB56 24 910073-1-553 15-567 AA39423, and AC068296, HFKKZ94 25 1163070-1-1318 15-1332 HHBGJ53 26 1187668-1-388 15-402 HHFJF24 27 1212624-1-2787 15-2801 HHFMM10 28 1178601-1-1857 15-1871 HHBPA42 29 901921-1-899 15-913 HHPSF68 30 1217052-1-2277 15-2291 HKABX13 31 1167182-1-970 15-984 HLTHG77 32 1162409-1-392 15-406 HLWBZ09 33 1179714-1-1940 15-1954 HLWEH54 34 1227713-1-4510 15-4524 HLYAA41 35 1188029-1-797 15-811 HLYDV62 36 1154065-1-805 15-819 HMCFB47 37 1151496-1-796 15-810 HMSOI20 38 1178817-1-2431 15-2445 HOENH55 39 1163460-1-612 15-626 HPIA01 40 1078178-1-926 15-940 HPJCT50 41 1201773-1-1983 15-1997 HPMFE91 42 1164740-1-1867 15-1881 HRAED5 43 1090522-1-645 15-659 HSMB19 44 1197925-1-2252 15-2266 HSYCY88 45 914775 1-1128 15-1142 HTEDW26 46 909749-1-1158 15-1172 HTEKD92 47 1090524-1-1447 15-1461 HTLDT08 48 1227127 1-2672 15-2686 HTPDS90 49 1197926-1-1920 15-1934 HTPHM71 50 1194698-1-2017 15-2031 HULFAR12 51 1194702 1-1704 15-1718 HWAGP22 52 1150195 1-1716 15-1730 HWBCE37 53 906968 1-418 15-432 HWAJF60 54 1223499 1-2867 15-2881 HDQGS16 55 1075725 1-447 15-461 HDQDV69 56 937850 1-837 15-851 AA867783, AW392670, U46341, AL119457, AL119341, AW372827, U46346, AW384394, AW363220, AL119484, AL119497, AL119355, AL119319, AL119324, AL119443, Z99396, U46350, U46351, AL119363, AL119391, AL119444, AL134902, U46347, U46349, AL119483, AL119396, AL134528, AL119418, AL119335, AL119496, AL119439, AL042433, AL119522, AL042965, AL134524, AL119399, AL134920, AL037205, AL119401, U46345, AL134536, AL142132, AL119464, AL042450, AL042614, AL043029, AL134525, AL134538, AL142131, AL042551, AL042984, AL042975, AL042544, AL043019, AL042970, AL142134, AL042542, AL043003, AL119489, AF169035, AF085233, AB028436, AR054110, AB1671, AR066494, AR080234, and AR090799. HE6BK63 57 1153879-1-755 15-769 HFKDR14 58 974255-1-1721 15-1735 A1761729, AW162515, AW104395, AW268361, A1073443, N40162, A1832126, A1827518, AW297353, RS2045, A1342317, R71958, AF128625, AF021936, and AB032950. HFPER62 59 1152249-1-619 15-633 HAAA058 60 1091089 1-1309 15-1323 HADFK69 61 1091937-1-1603 15-1617 HDPM062 62 1162329-1-1123 15-1137 HDPM065 63 1226282-1-2479 15-2493 HDPUY72 64 1228285-1-3040 15-3054 HADTFJ87 65 1154640-1-826 15-840 HEBTB94 66 1178794 1-1913 15-1927 HECU855 67 1228113-1-3332 15-3345 HEGDA65 68 1178633-1-1803 15-1817 HEGB58 69 1197907 1-1245 15-1249 HELHC48 70 956003-1-803 15-817 HEQHQ90 71 1212646-1-2609 15-2623 HFKHA18 72 1152242-1-1055 15-1069 HFKMA10 73 964258-1-960 15-974 HHBFM91 74 1092116 1-901 15-915 H1201773 75 912715 1-950 15-964 AC012171, AC012171, AC012171, AC009095, AC009095, AC009095, AC005346, AC005346, and AC005346. HMCEI38 76 11344410 1-613 15-627 HHWDJ68 77 1154790 1-1350 15-1364 HOEOL58 78 1078090-1-778 15-792 HRAE651 79 1162856 1-1075 15-1089 HSHAV32 80 1160388-1-2589 15-2603 HTPDE66 81 971281-1-479 15-493 HTPDV73 82 997559 1-411 15-425 HTPHC33 83 1163871-1-1714 15-1728 HUFDF58 84 1224609-1-2404 15-2418 HUVFV X92 85 1225329 1-428 15-442 HWAEG71 86 1182321-1-1471 15-1485 HWAHD49 87 1228064-1-1365 15-1379 HWLG031 88 1178825-1-2007 15-2021 HWLKF25 89 1089052-1-1097 15-1111 H2CBH49 90 963811-1-470 15-484 AA307462, AA036880, AL133047,

D89677, AC068243, and AC068243. HAGDN53 91 1092161 1-1702 15-1716 HAMFM39 92 971347 1-4593 15-4607
 A1951619, A1814592, A1745391, A1922346, AA426190, AW105735, AW297557, A1928667, A1971855, AA227634,
 A18028756, AA 151872, A1577072, A1020419, AW176248, AW295401, A1659079, AA149658, AA425159, A1765117,
 A1870033, AW194075, AA233413, A10102818, R61588, AA365664, AA365663, A6011170, R61532, AA357346,
 AA551861, A1660231, A1467732, Z99396, AW392670, AL119324, AL119319, U46350, A16351, AL119457, AL119484,
 AL119391, U46347, AW372627, AL119522, AL119439, AL119335, AW384394, AL119483, AW363220, AL119363,
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 A94046, A94054, I63120, AR067733, AR064322, AR064323, AR064320, AR064321, A32110, A94048, A94061, A94045,
 AR038321, A83642, AR019094, A83643, A70359, A92666, AR038307, A92668, A92667, I49890, A92665, A92061,
 A92080, A92077, A92078, A92079, AR018924, AR018923, A48774, A48775, AR000006, AR015960, AR015961,
 AR000007, A91752, A91751, AR051652, A85308, AR068508, AR068510, AR068509, I91969, A91754, 158322, 158323,
 AR003585, A63067, A51047, A63064, A63072, AR031375, AR068507, A60213, AR068506, AR062871, A44171,
 AR068550, A23373, AR068551, A49700, A60207, A60208, A29109, A32111, 158669, A58521, AR031374, I07209,
 I07249, A63954, AR051651, AR019097, AR019098, AR019096, AR029417, I77227, AR020199, AR020200, AR001287,
 AR020198, AR020197, I89986, AR051957, AR029418, AR067731, AR067732, Y14971, A93444, A46342,
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